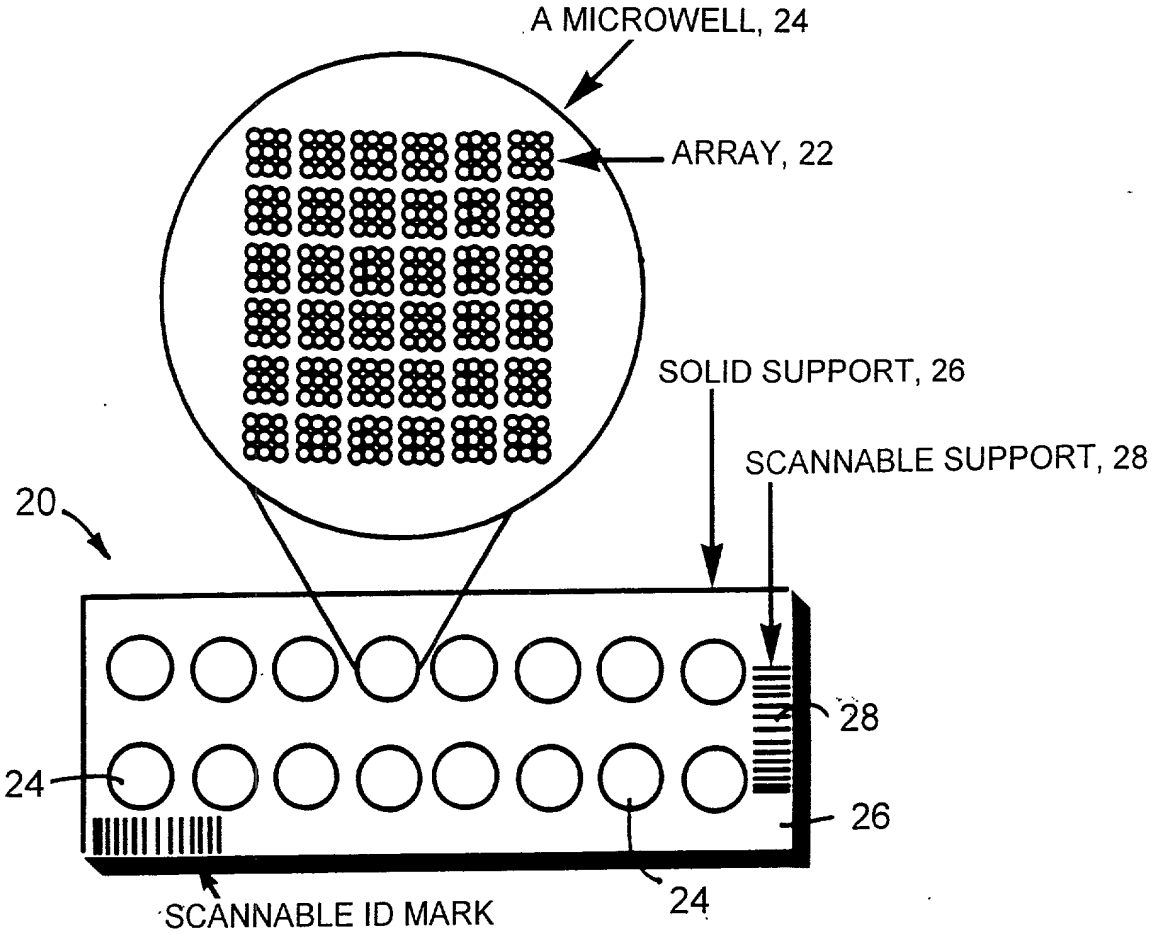

A MICROWELL, 24
ARRAY, 22
SOLID SUPPORT, 26
SCANNABLE SUPPORT, 28
20
28
24
26
SCANNABLE ID MARK
24

FIG. 1A

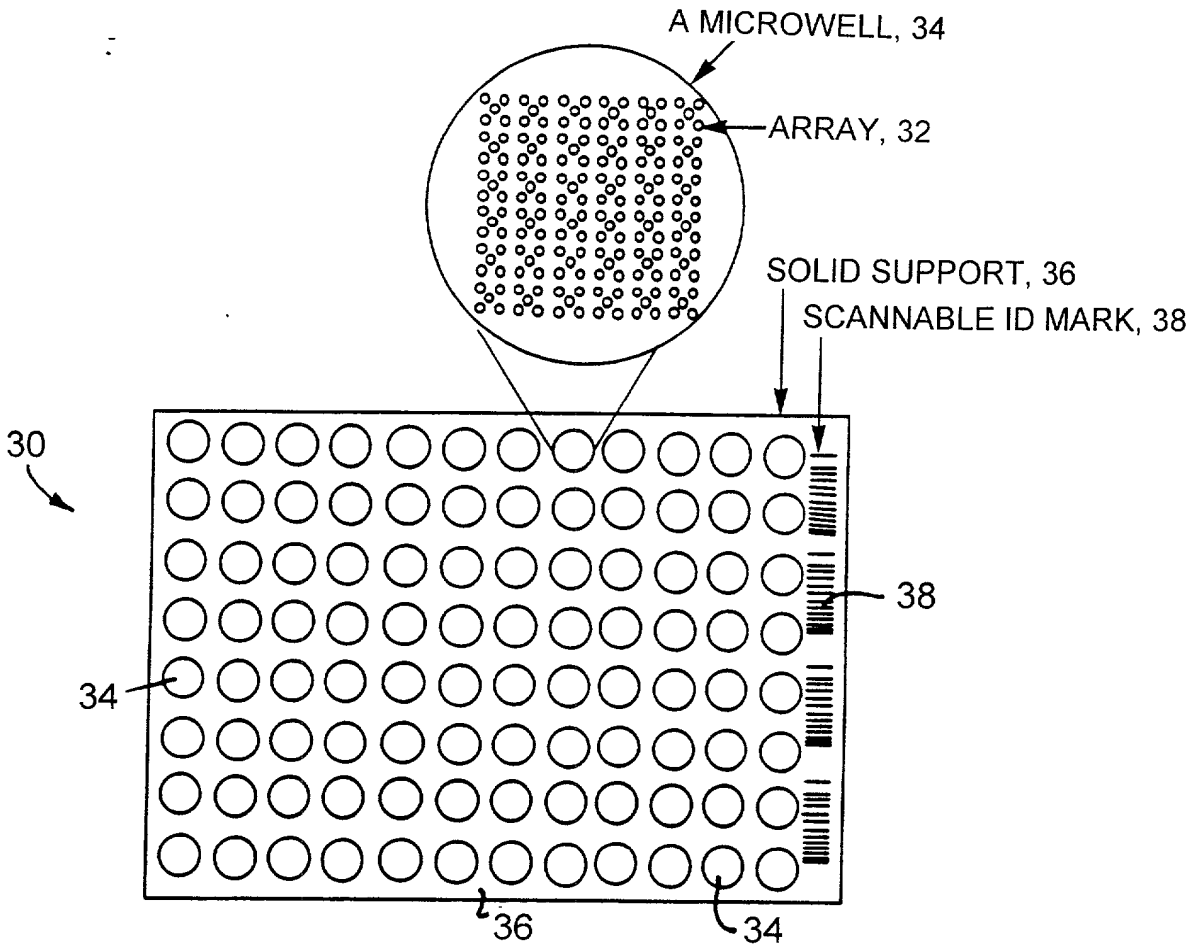

A MICROWELL, 34
ARRAY, 32
SOLID SUPPORT, 36
SCANNABLE ID MARK, 38
30
38
34
36
34

FIG. 1B

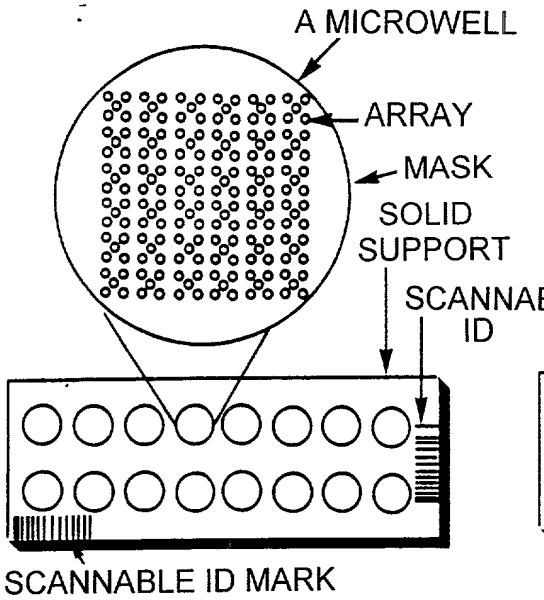


FIG. 2A

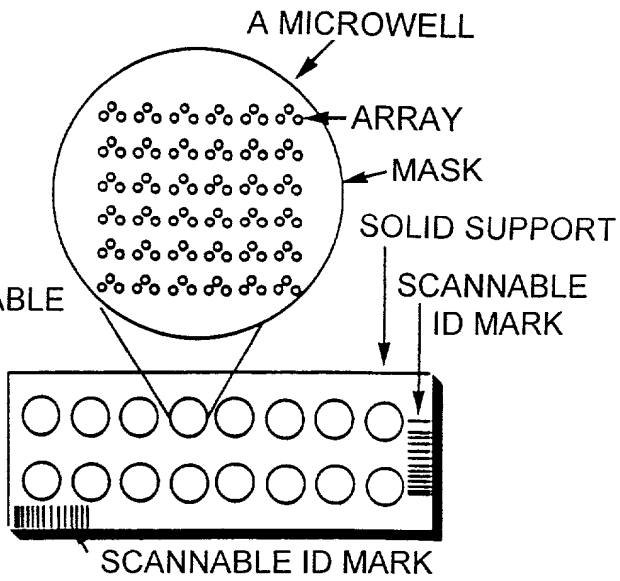


FIG. 2B

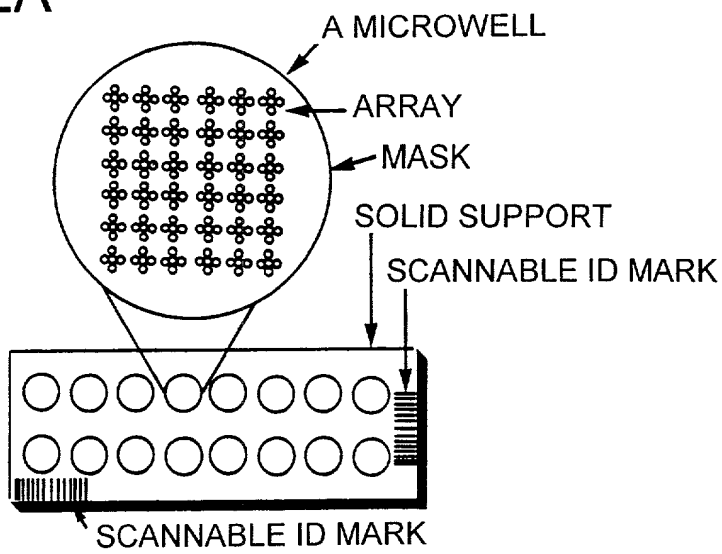


FIG. 2C

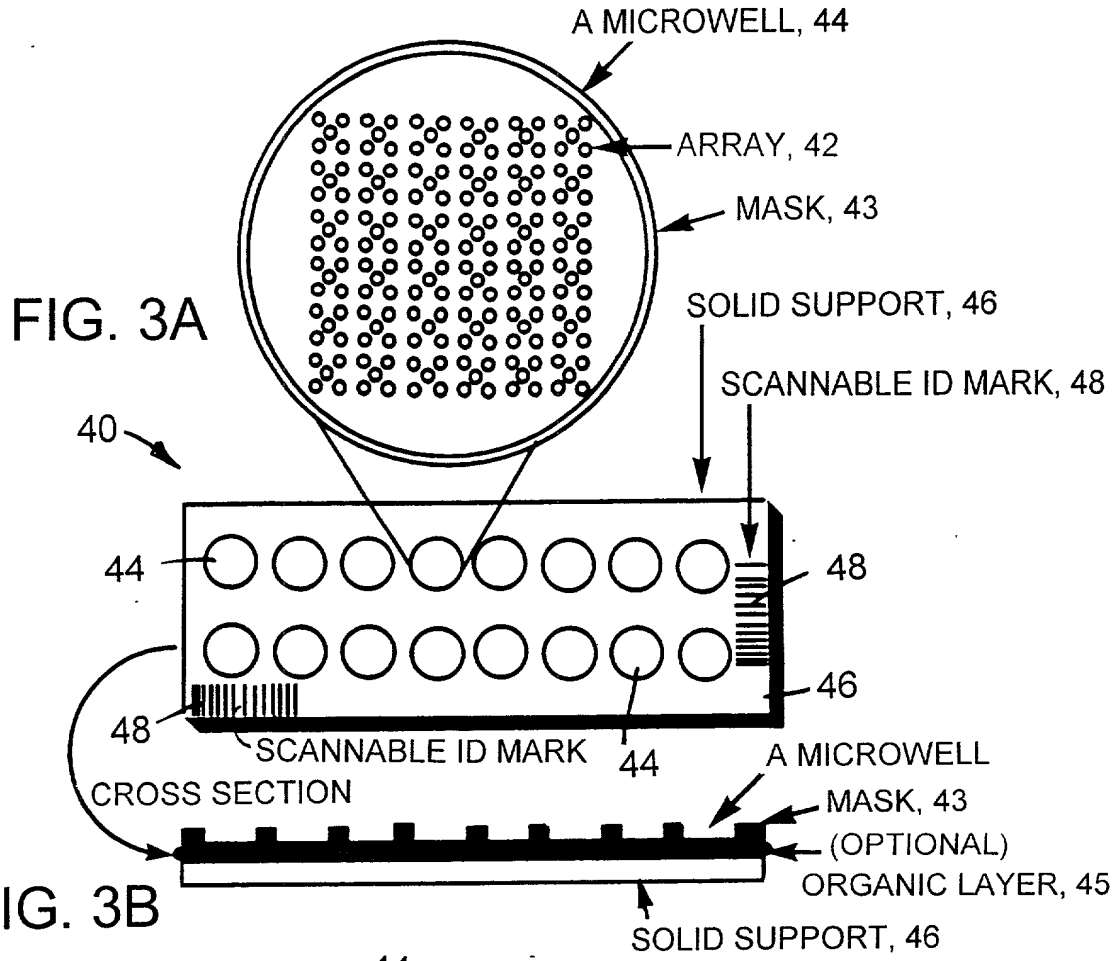


FIG. 3A

FIG. 3B

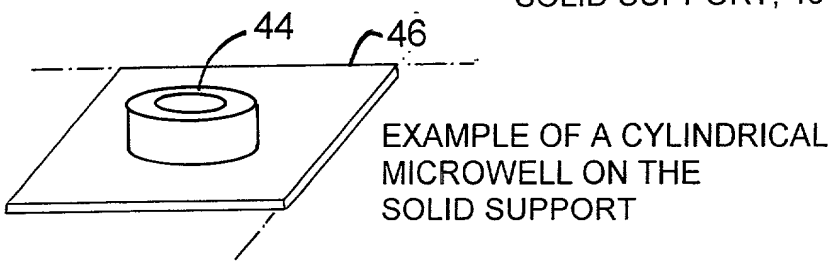


FIG. 3C

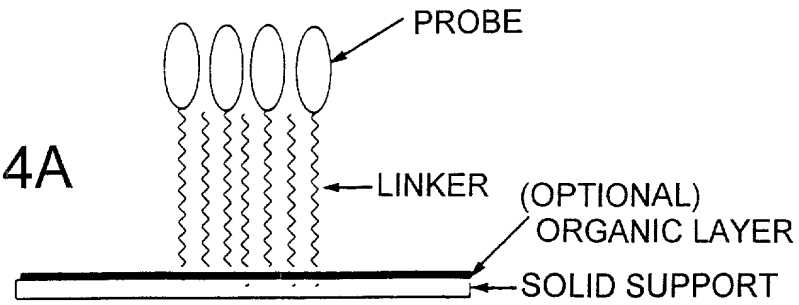


FIG. 4A

ATTACHING PROBES TO SOLID-SUPPORT WITH LINKERS OF THE SAME LENGTH RESULTS IN LOWER DENSITY OF PROBE ATTACHMENT

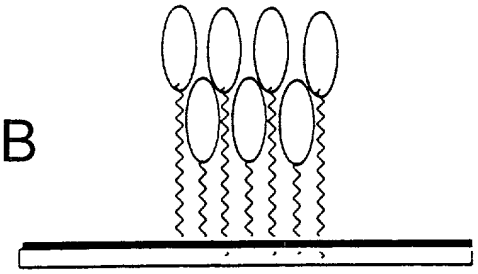


FIG. 4B

ATTACHING PROBES TO SOLID-SUUPORT WITH LINKERS OF DIFFERENT LENGTHS RESULTS IN MUCH HIGHER DENSITY OF PROBE ATTACHMENT

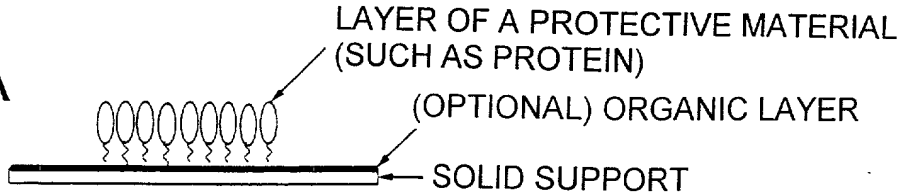
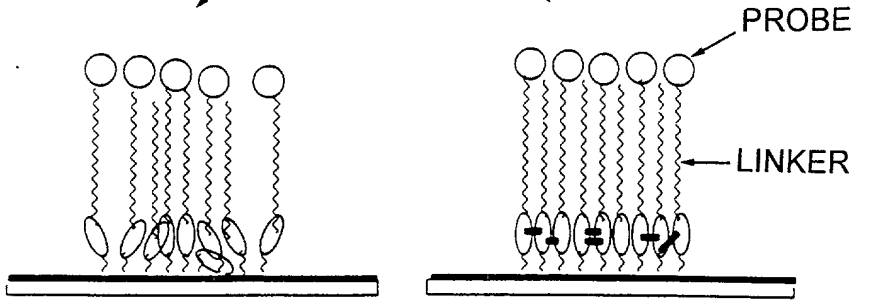


FIG. 5A

A LAYER OF PROTECTIVE MATERIAL IS LAID WITH SMALL LINKERS

NO CROSS-LINKING

CROSS-LINKING



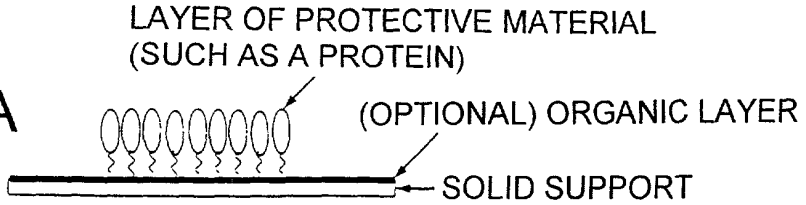
FINAL PROBE LINKING MAY RESULT IN A DIS-ORDERING ARRAY

FIG. 5B

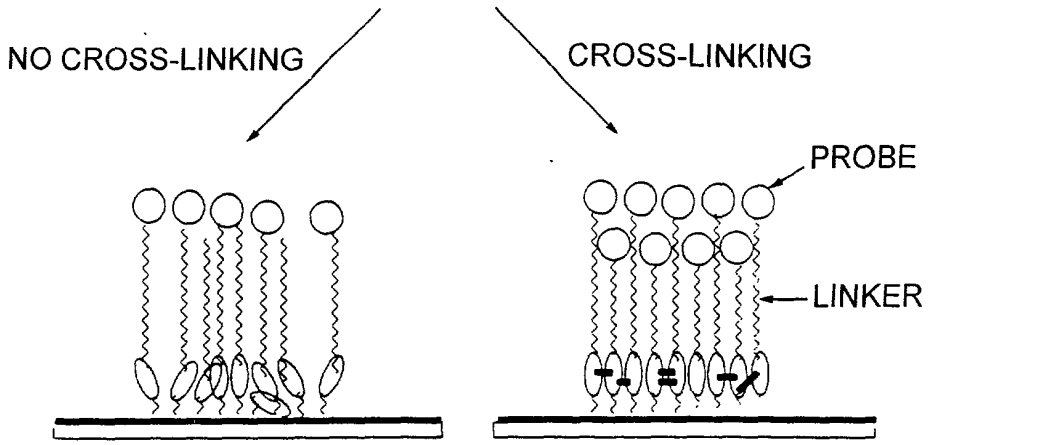
FINAL PROBE LINKING MAY RESULT IN AN ORDERIED ARRAY

FIG. 5C

FIG. 6A



A LAYER OF PROTECTIVE MATERIAL IS LAID WITH SMALL LINKERS



FINAL PROBE LINKING MAY RESULT IN A DIS-OREDERED ARRAY

FIG. 6B

FINAL PROBE LINKING MAY RESULT IN AN ORDERED ARRAY

FIG. 6C

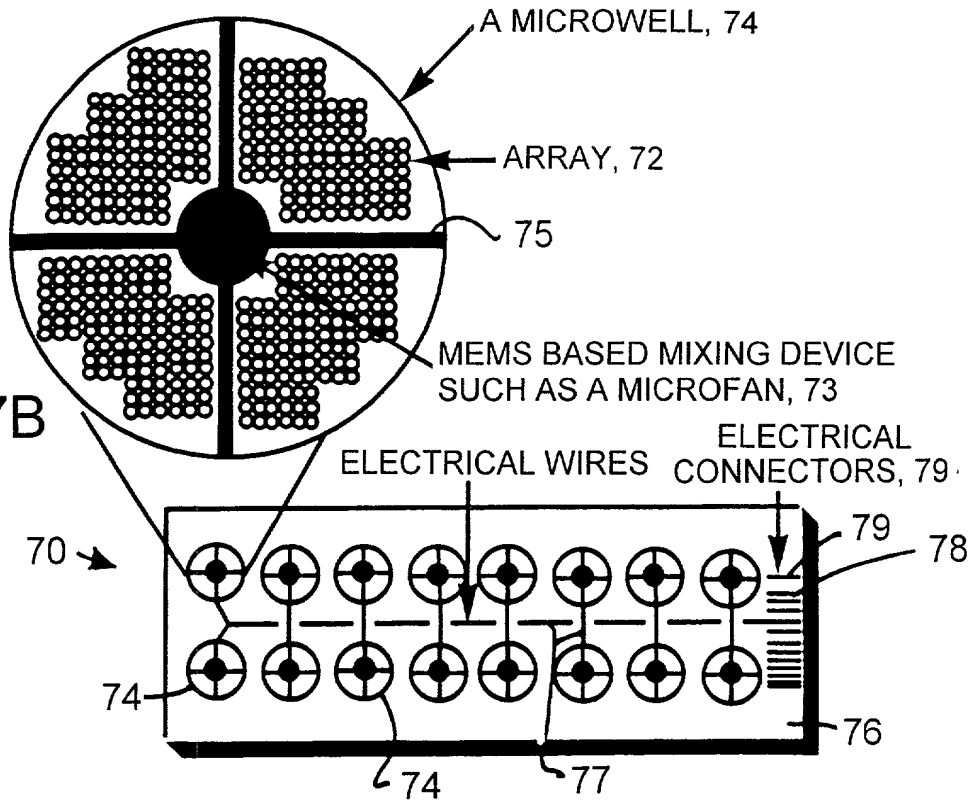


FIG. 7B

FIG. 7A

DOCKET.COM

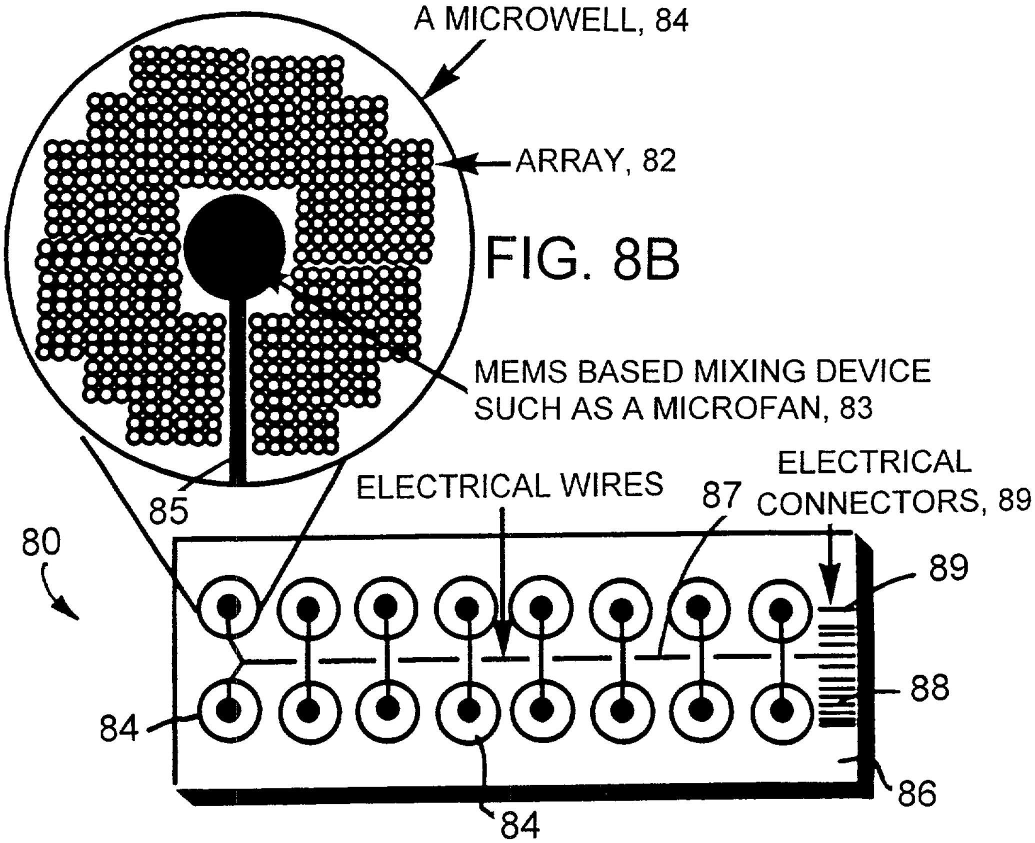


FIG. 8B

FIG. 8A

09996056 .032802

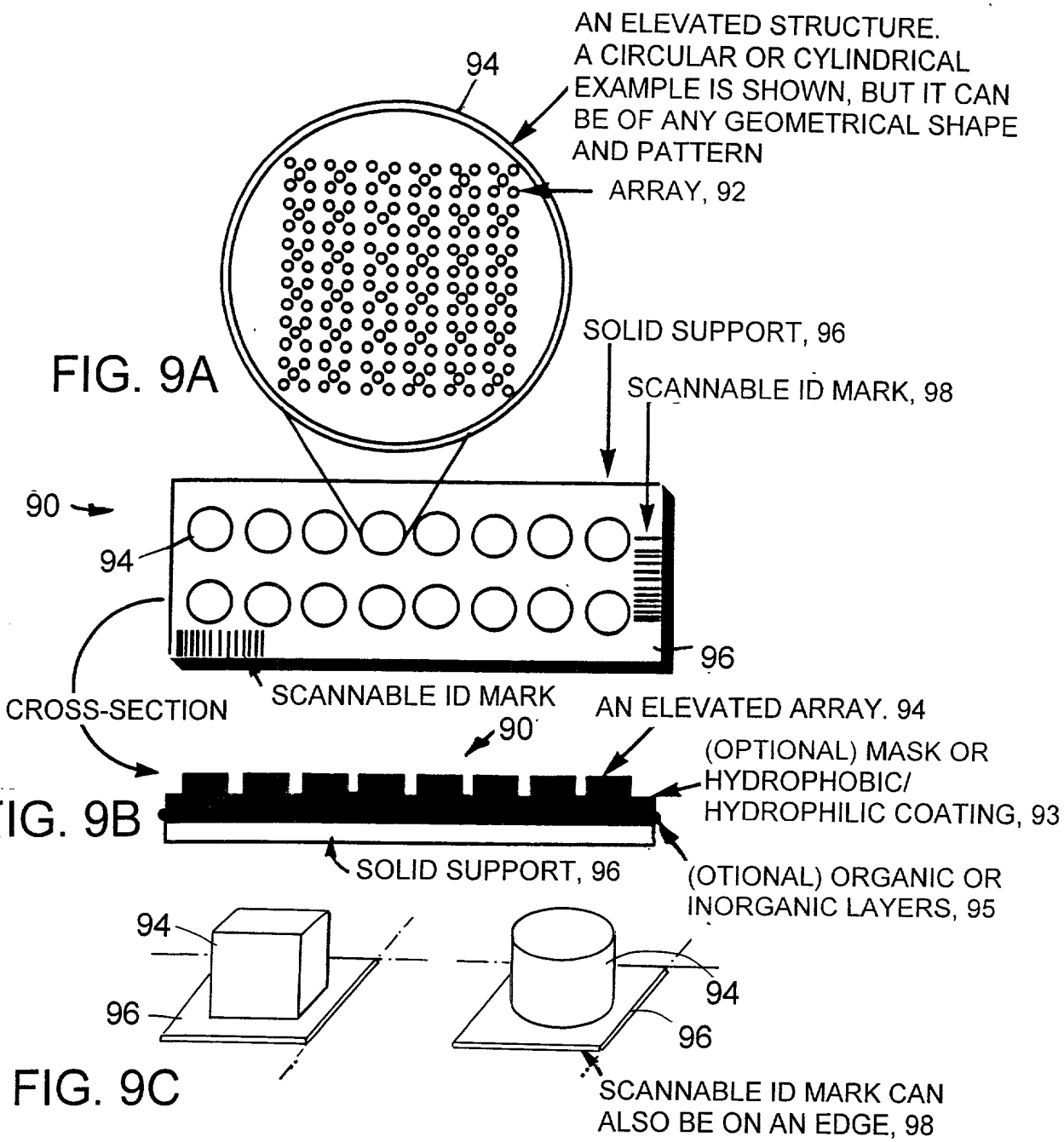


FIG. 9A

FIG. 9B

FIG. 9C

EXAMPLES OF ELEVATED STRUCTURES ON SOLID SUPPORT.
THE STRUCTURES CAN BE CYLINDRICAL OR CUBOID OR ANY
OTHER GEOMETRICAL SHAPE

Replacement Sheet
09/996,056

TWO VIEWS OF TWO TYPES OF "INVERTED ARRAYS"

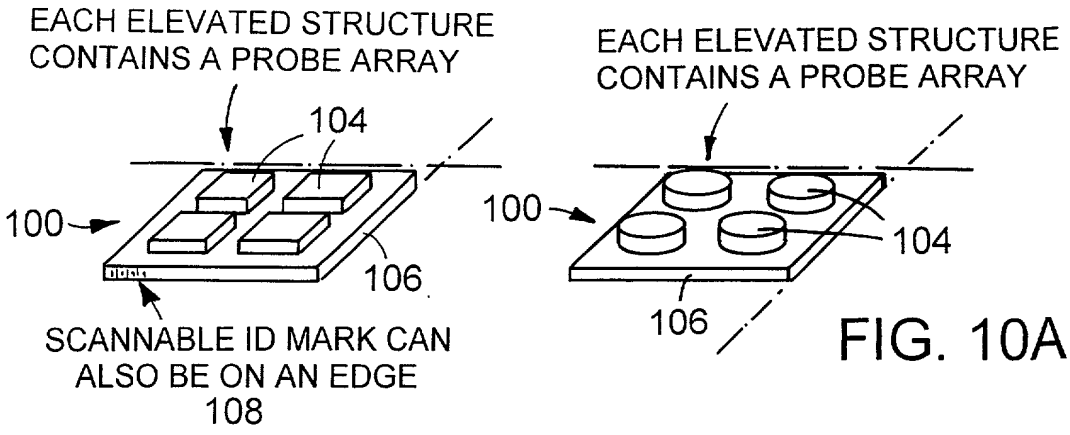


FIG. 10A

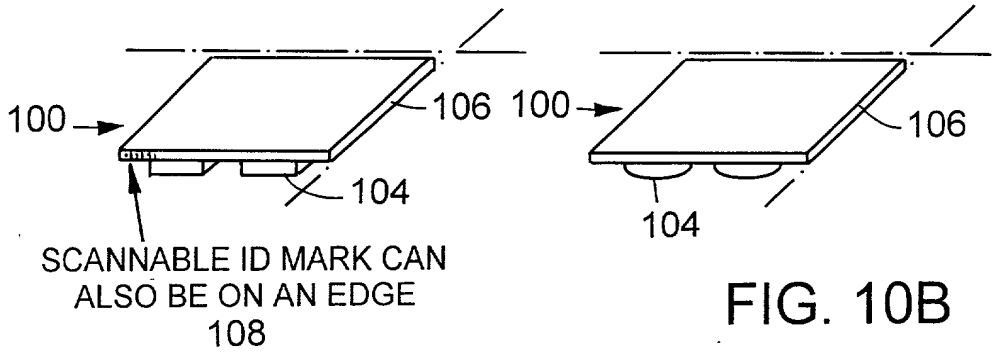


FIG. 10B

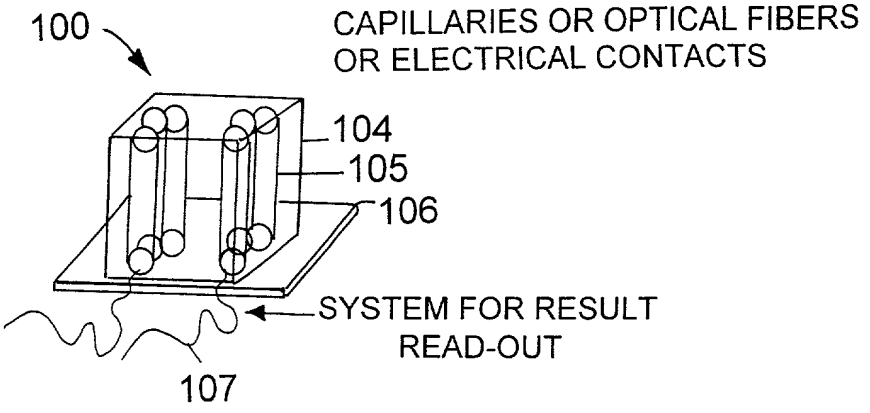


FIG. 10C

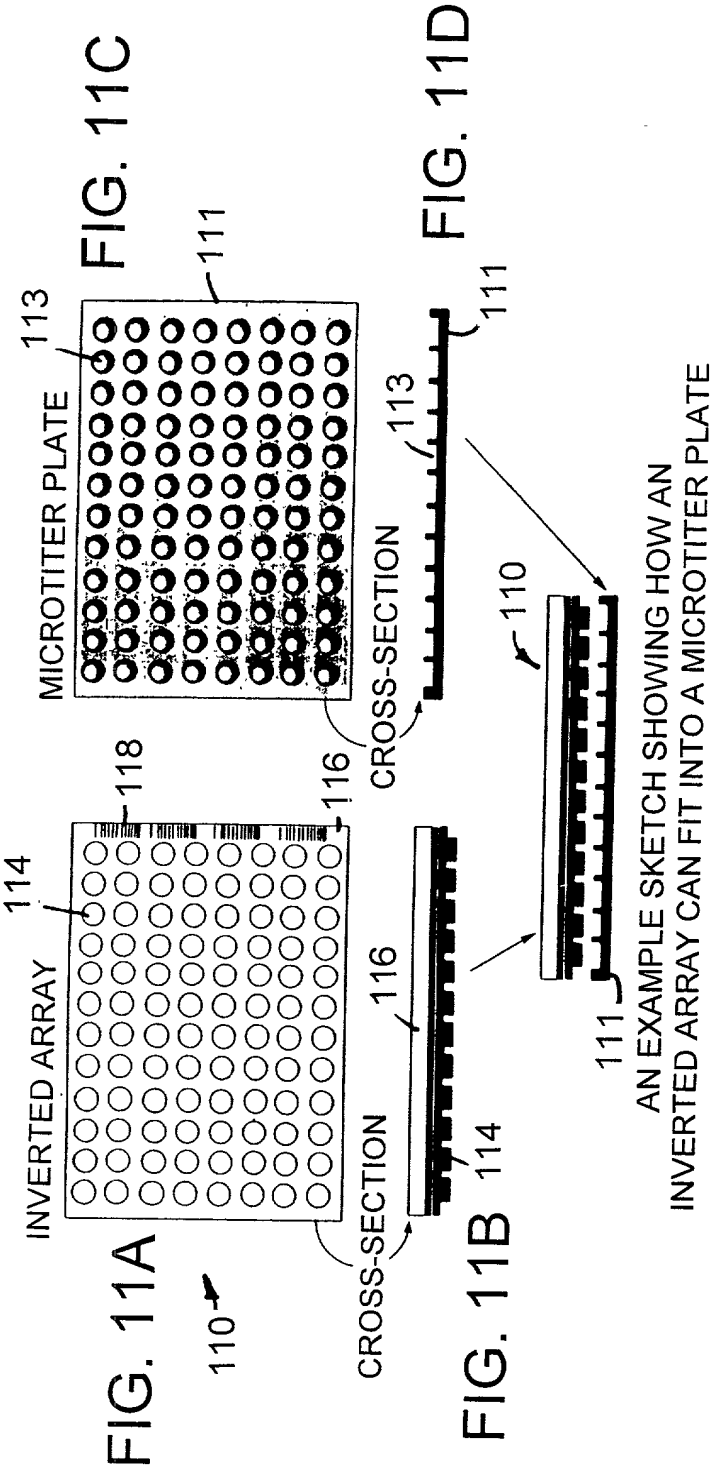


FIG. 11A

FIG. 11B

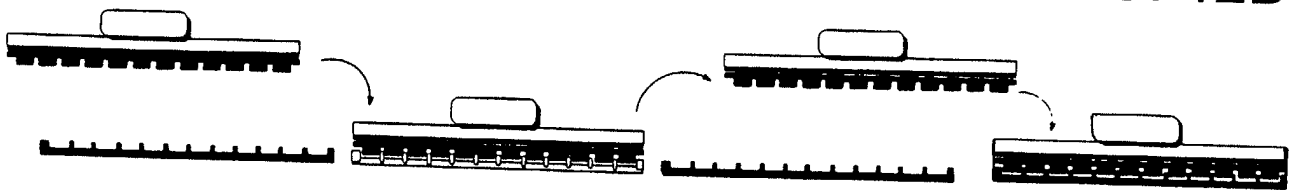
FIG. 11C

FIG. 11D

FIG. 11E

208260 " 95096460

FIG. 12A FIG. 12B FIG. 12C FIG. 12D



THE "INVERTED ARRAY" CAN BE MOVED FROM ONE REACTION VESSEL TO ANOTHER. IT CAN BE MOVED EITHER USING A BUILT-IN HANDLE OR USING A VACUUM SUCTION DEVICE OR ANY OTHER MECHANISM. THE PROCESS CAN BE DONE MANUALLY OR ROBOTICALLY AND THE ASSAY PROCEDURE CAN BE EASILY AUTOMATED. THIS SCHEMATIC SHOWS AN EXAMPLE OF ONE SUCH PROCESS.

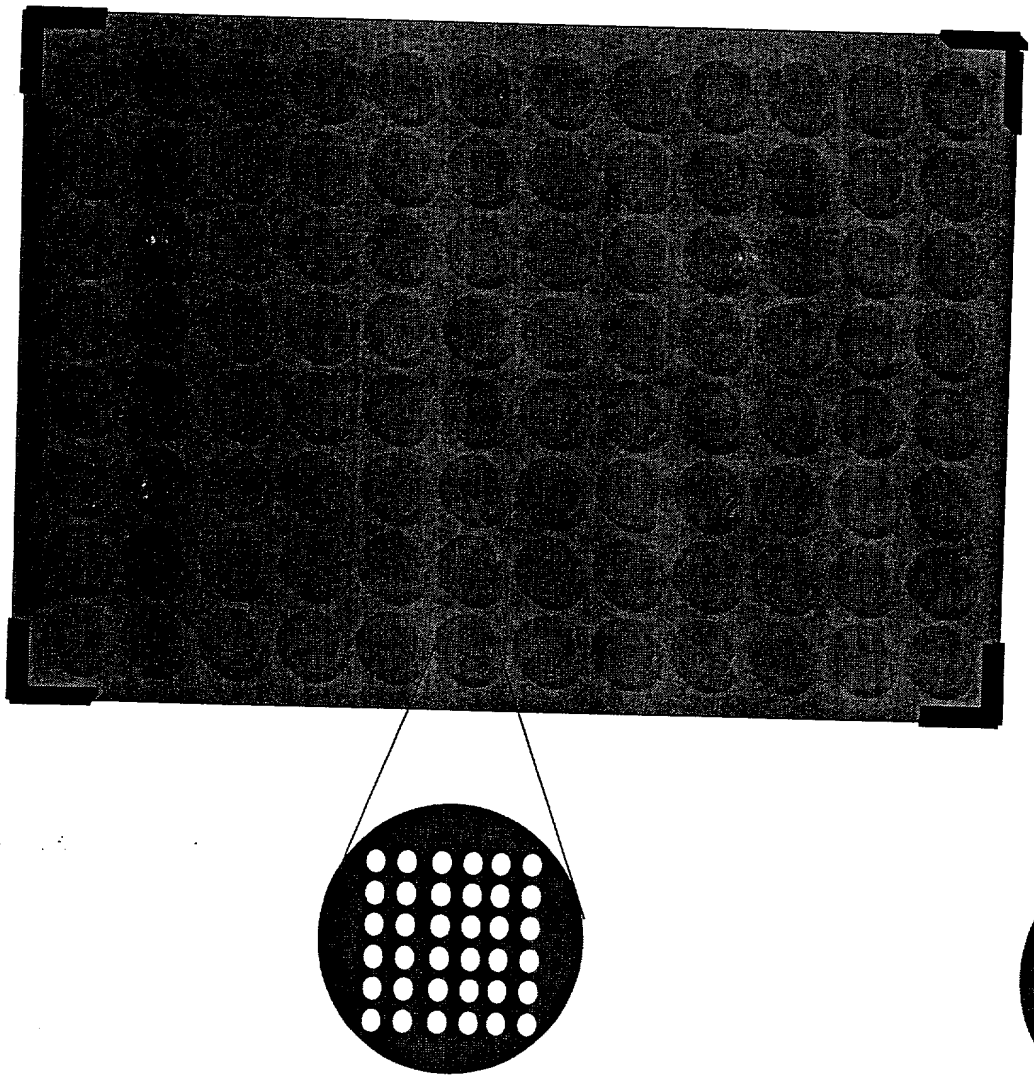


FIG. 13A

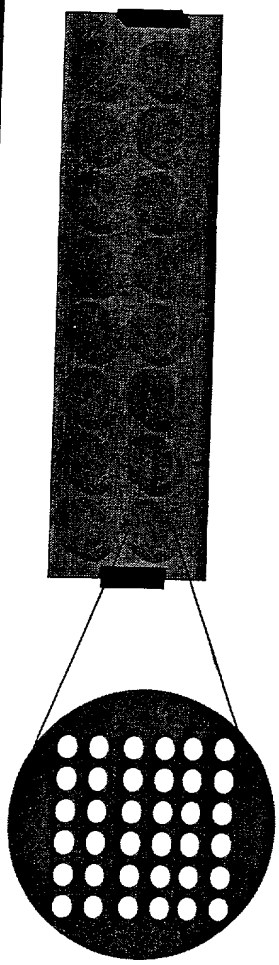


FIG. 13B

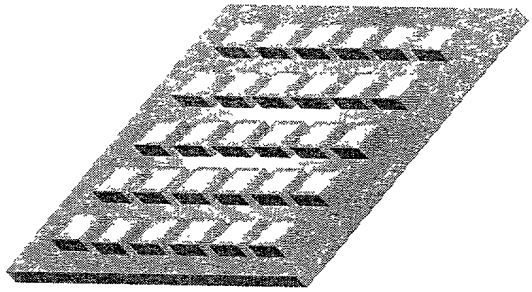


FIG. 13C

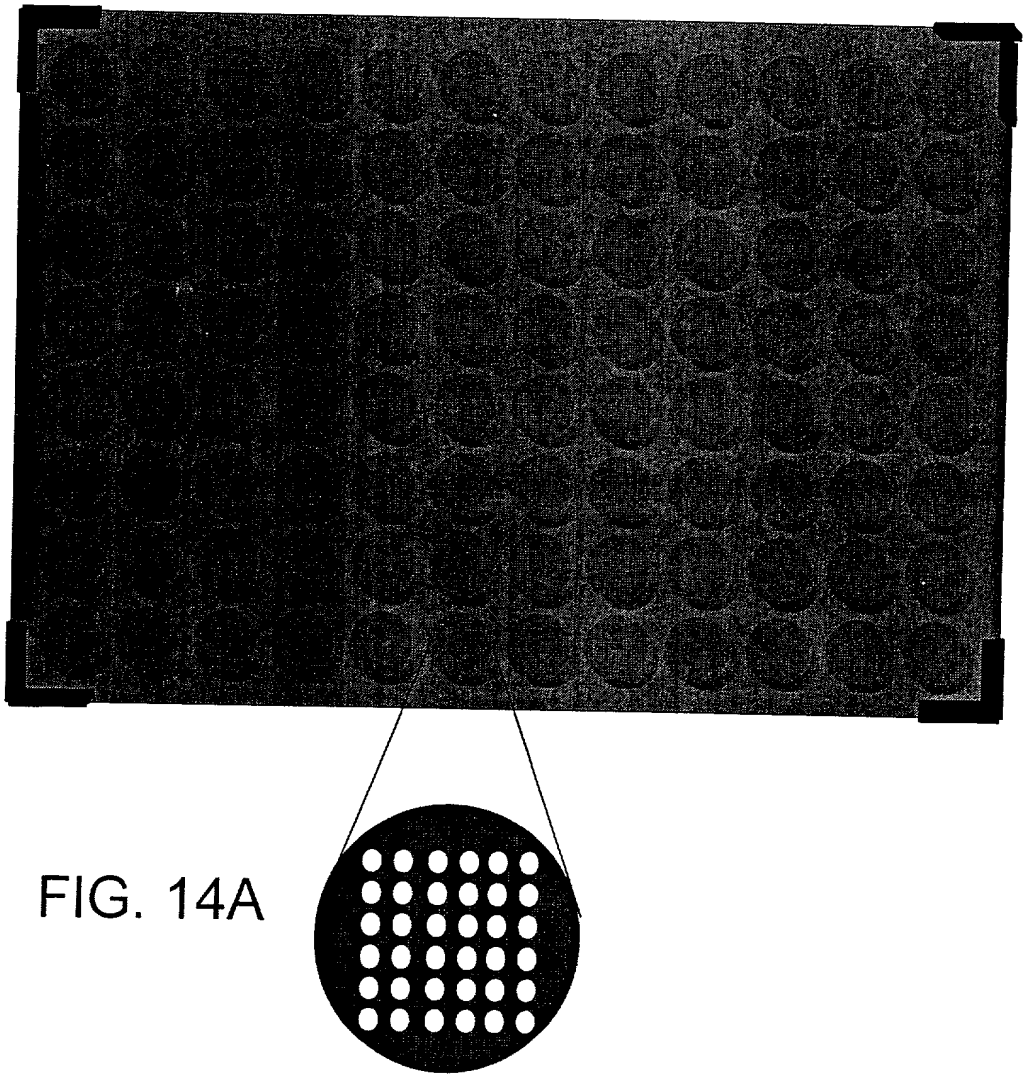


FIG. 14A

FIG. 14B **Elevated sub-structure**

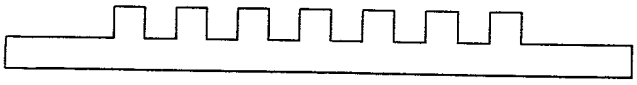


FIG. 14C **Planar sub-structure**

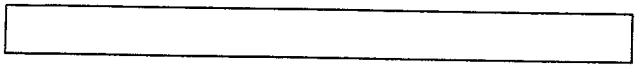
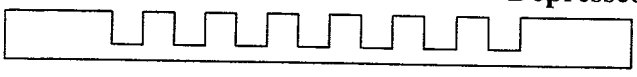


FIG. 14D **Depressed sub-structure**



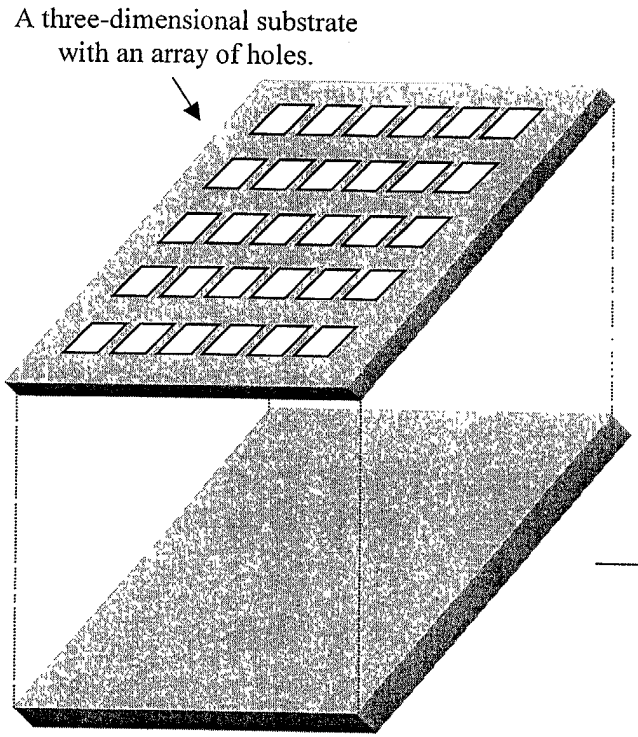


FIG. 15A

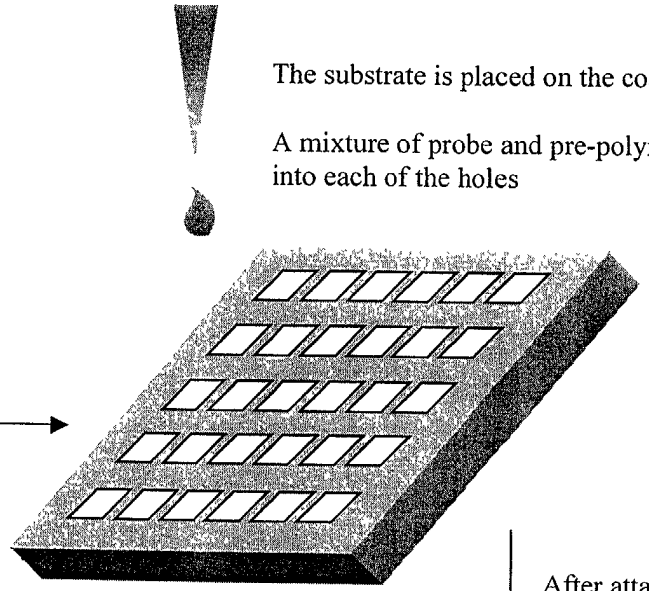


FIG. 15B

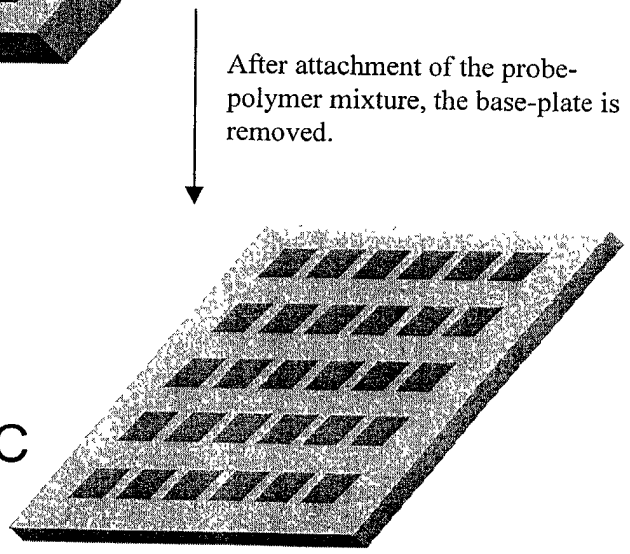


FIG. 15C

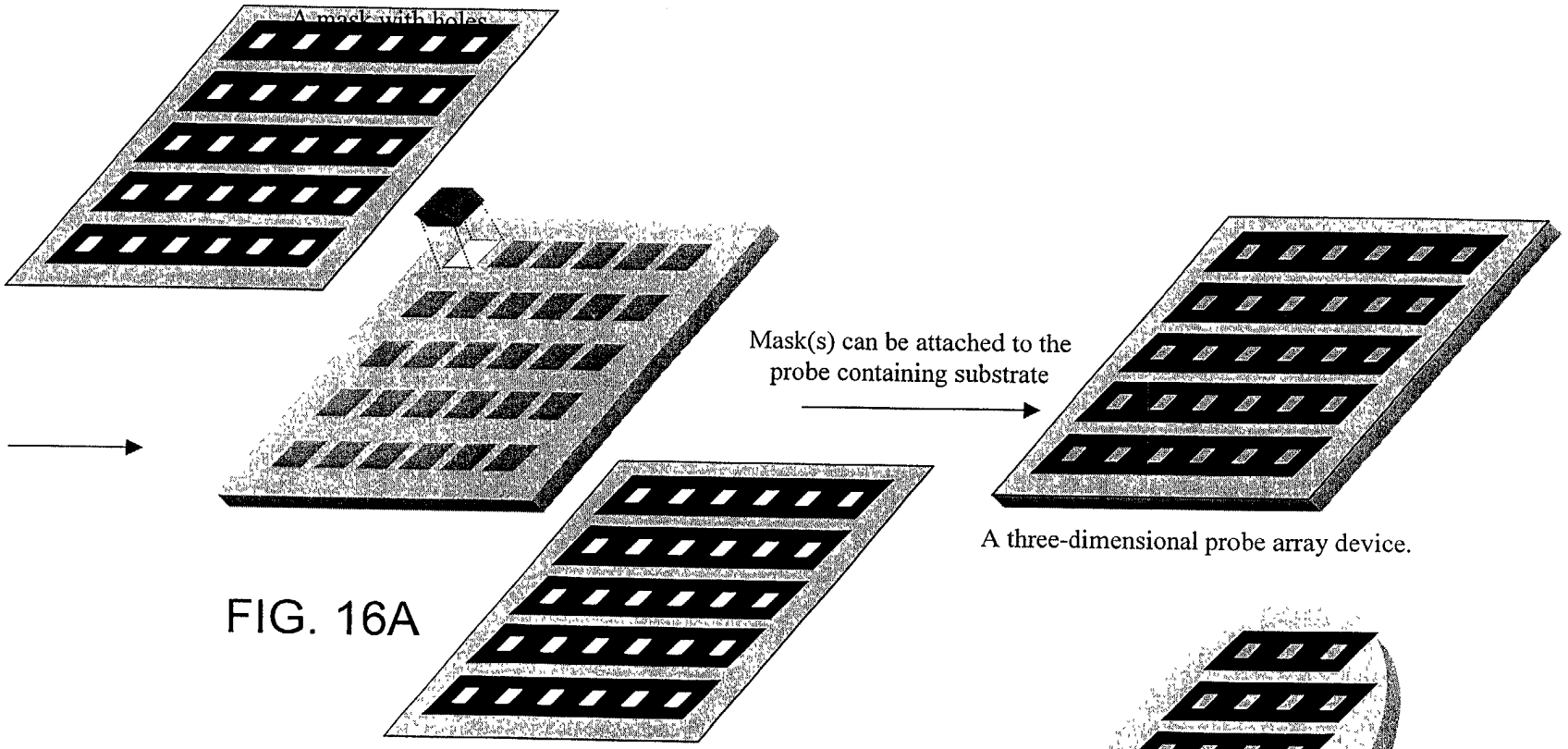


FIG. 16A

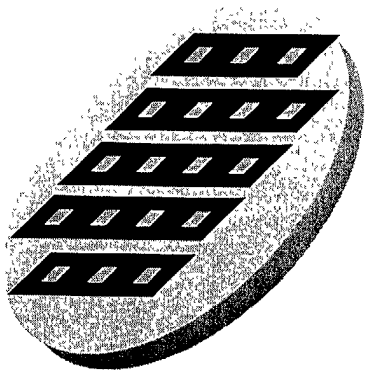


FIG. 16B

FIG. 16C

The microarray biochip can
Also be housed in a sealed chamber.

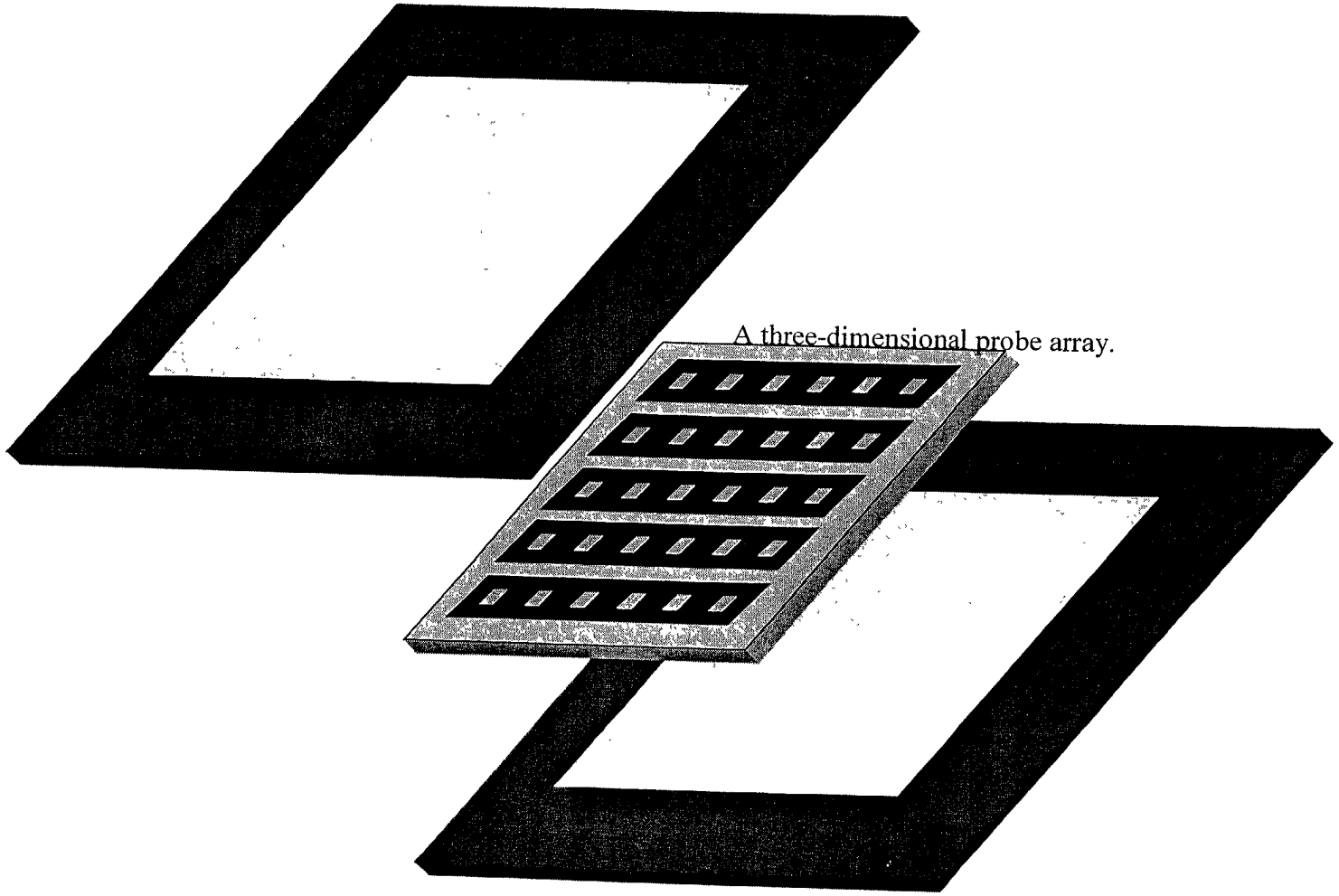


FIG. 17

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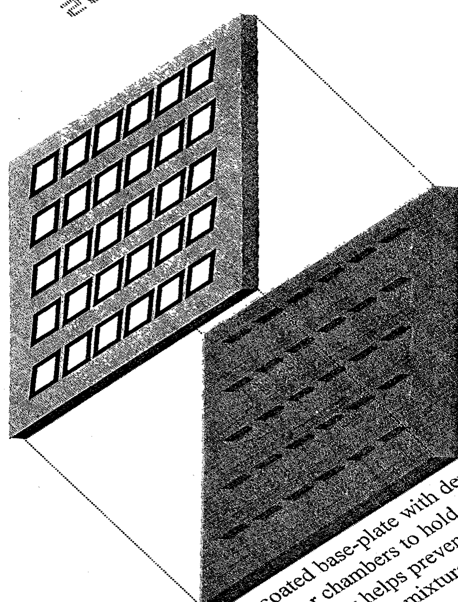


FIG. 18A

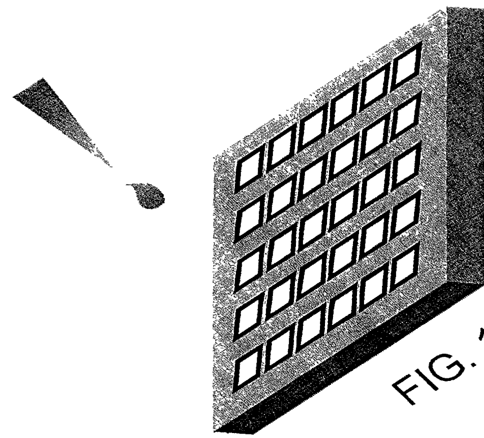


FIG. 18B

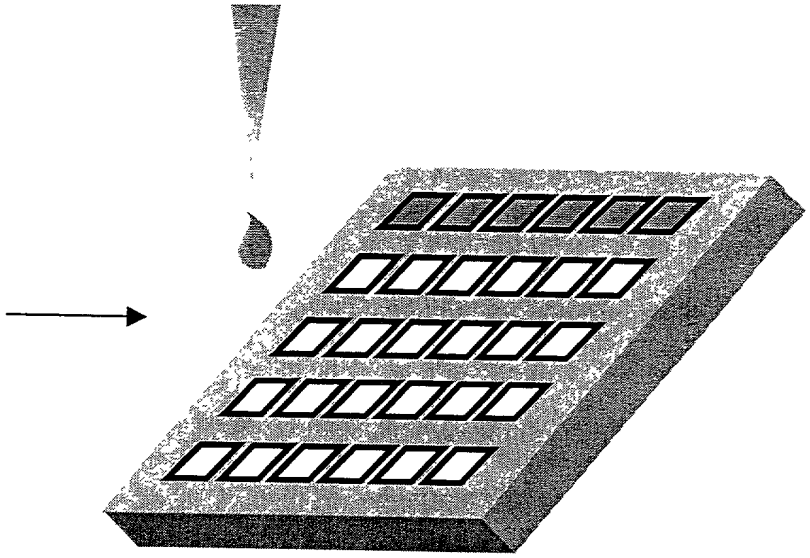
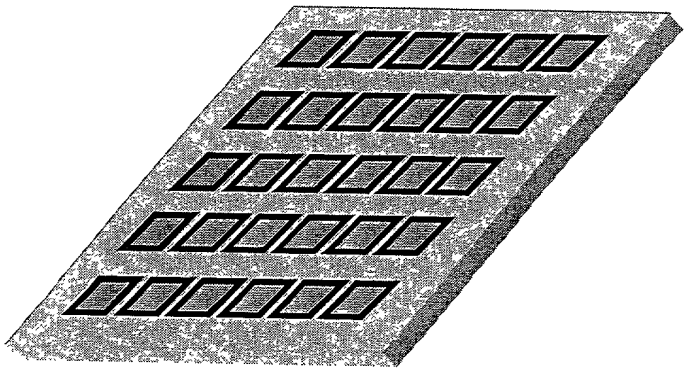


FIG. 19A



Another implementation of 3D porous biochip

FIG. 19B

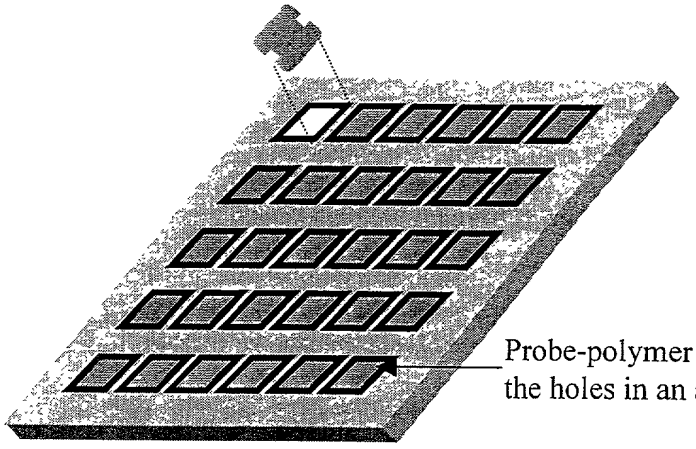


FIG. 19C

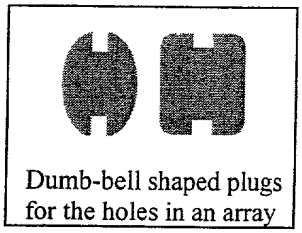
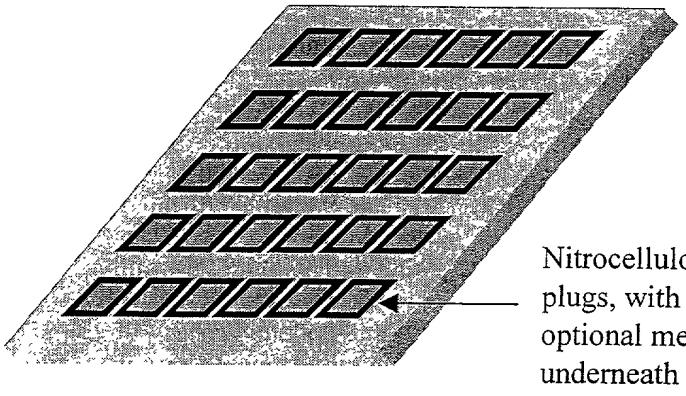


FIG. 19D



Two examples of the types of material that can be used to manufacture the 3D porous array

FIG. 19E

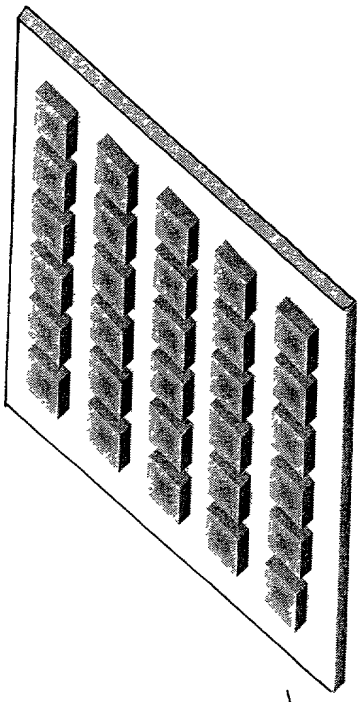


FIG. 20A

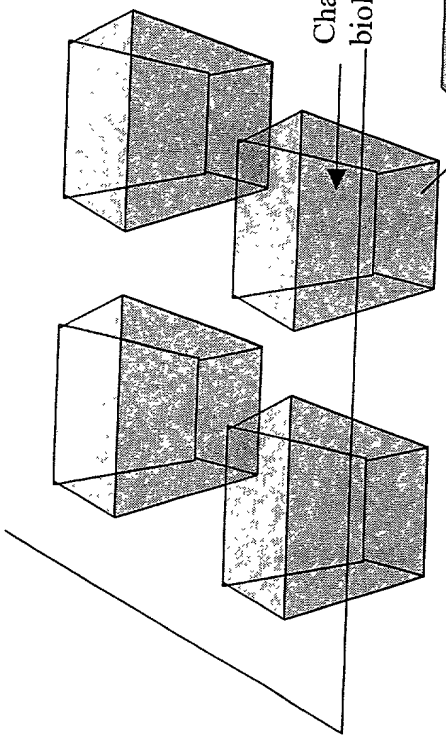


FIG. 20B

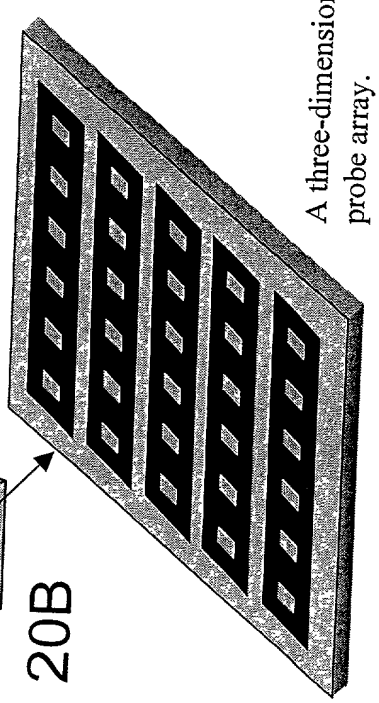


FIG. 20C

The microarray biochip can also be housed in a sealed hand-held or Point of Care device.

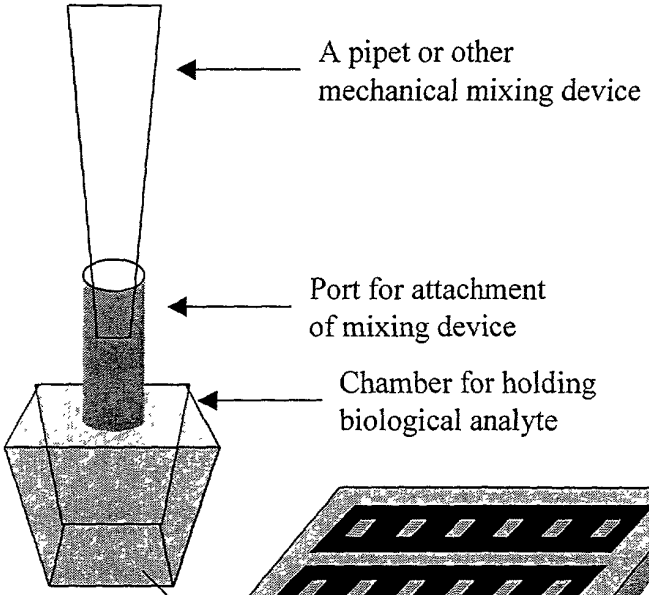


FIG. 21A

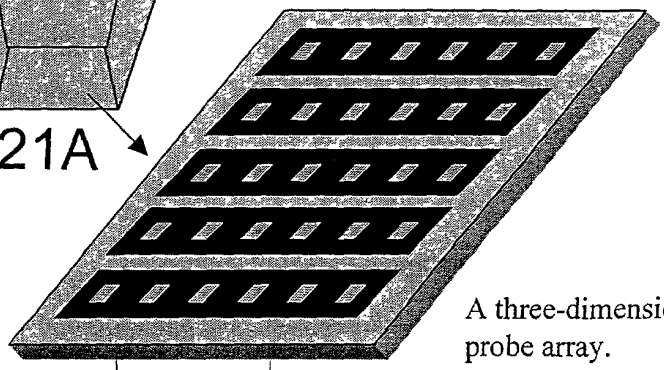


FIG. 21B

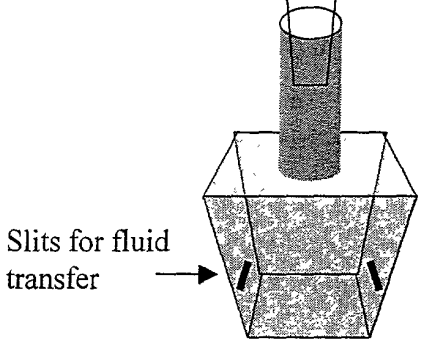


FIG. 21C

Another implementation of the chamber for holding biological analyte

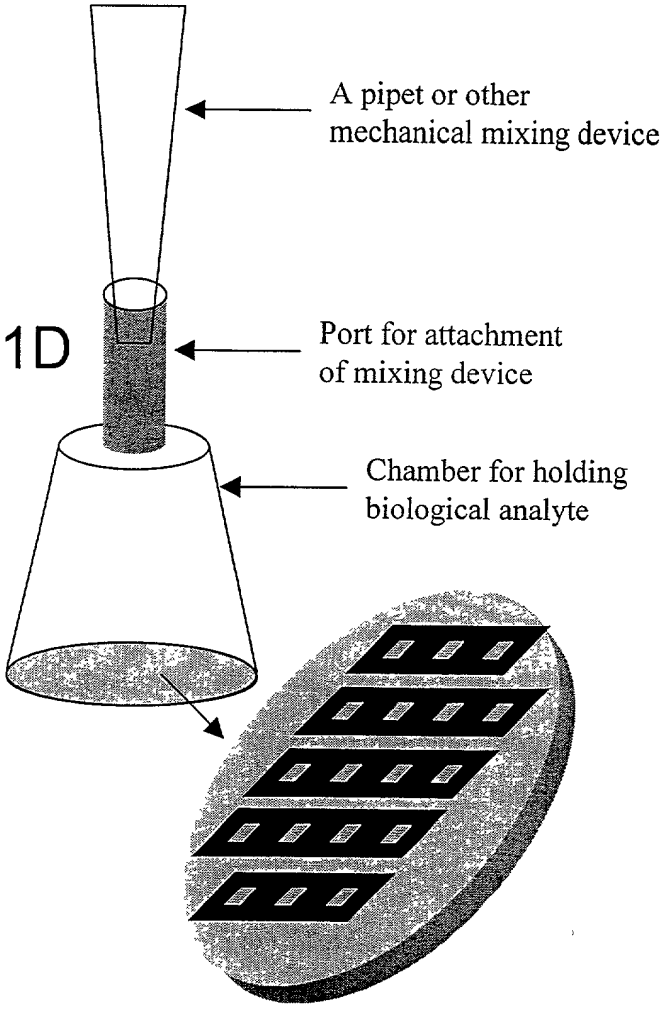


FIG. 21D

A three-dimensional probe array.

FIG. 21E

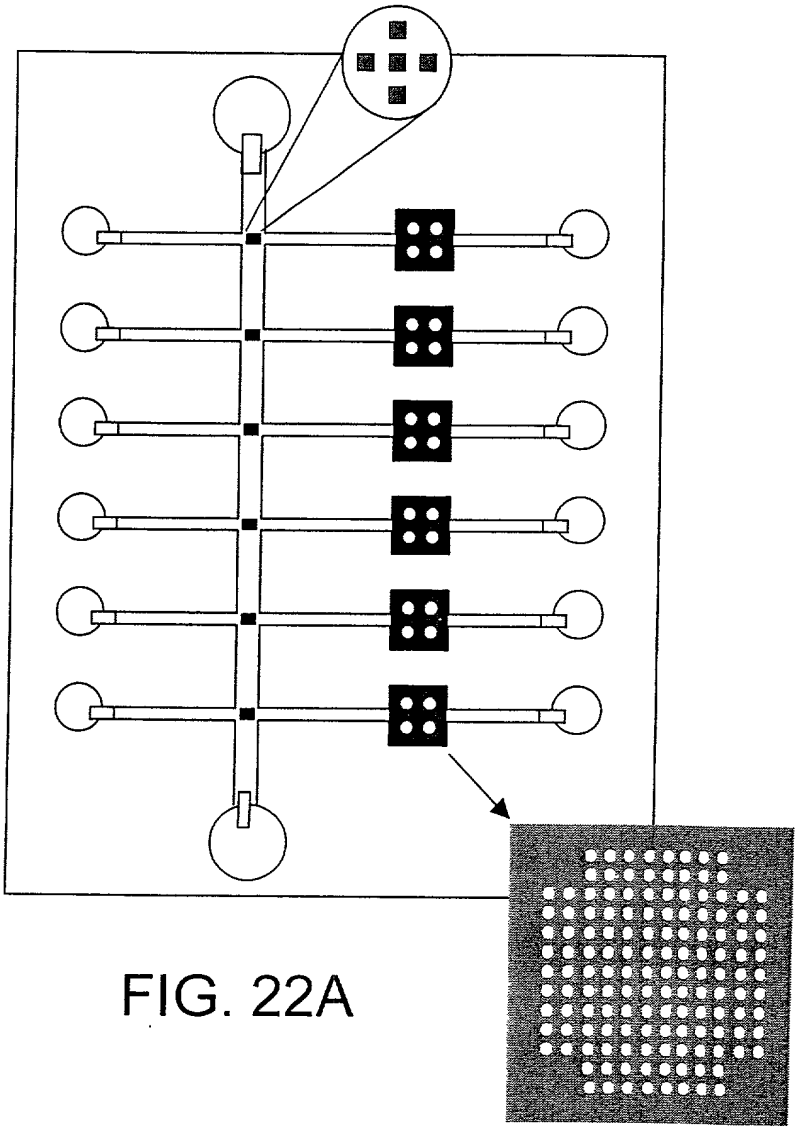


FIG. 22A

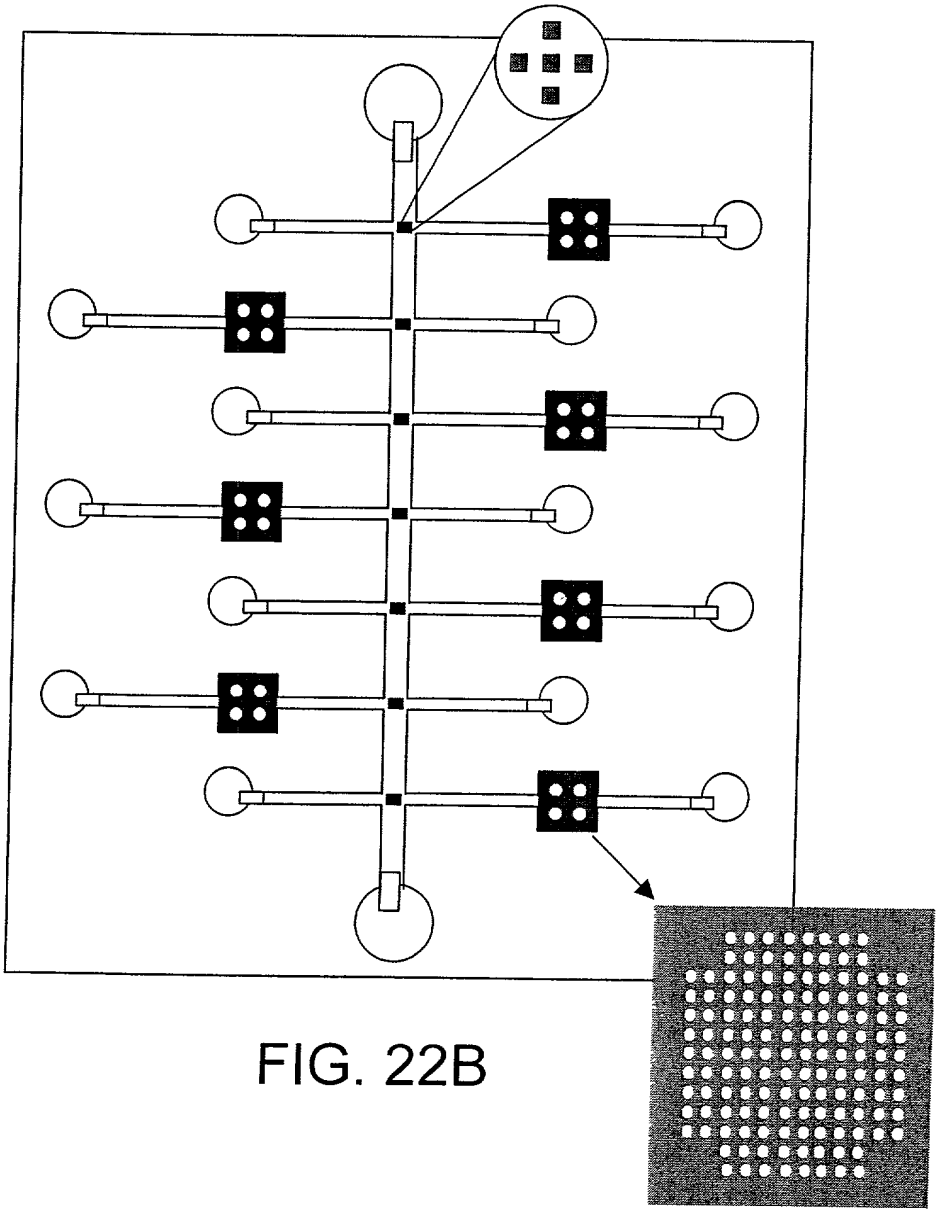


FIG. 22B

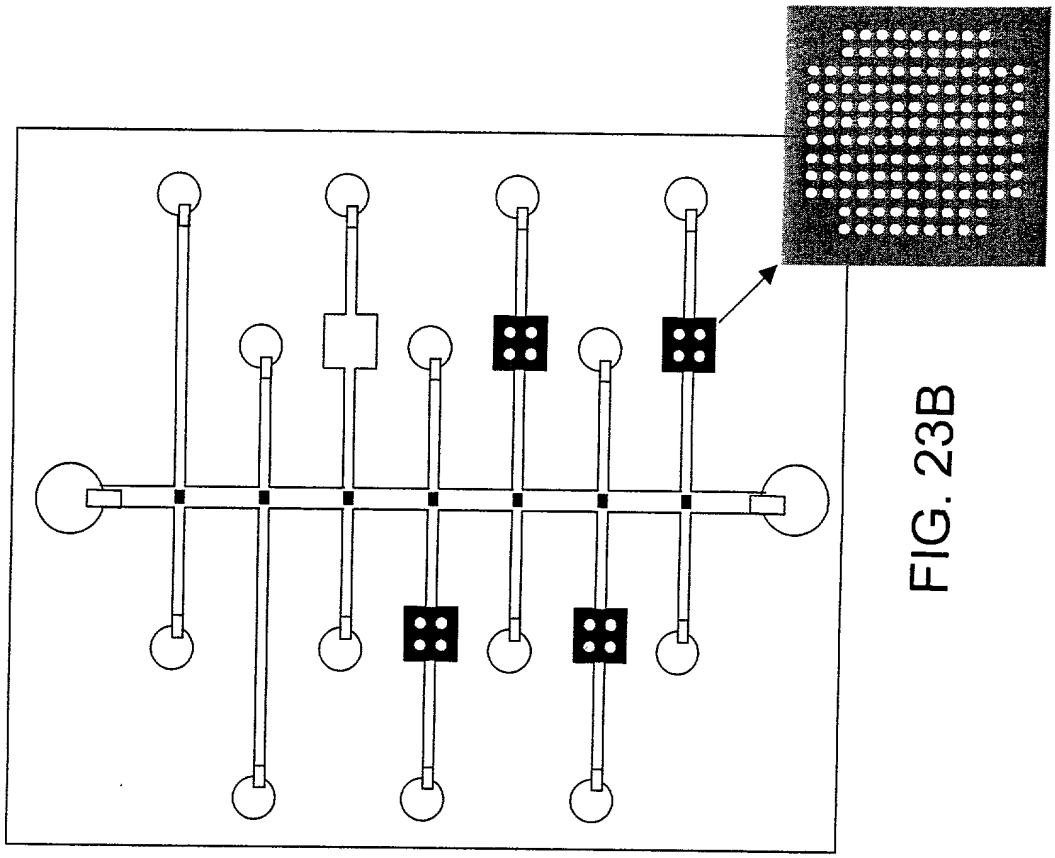


FIG. 23B

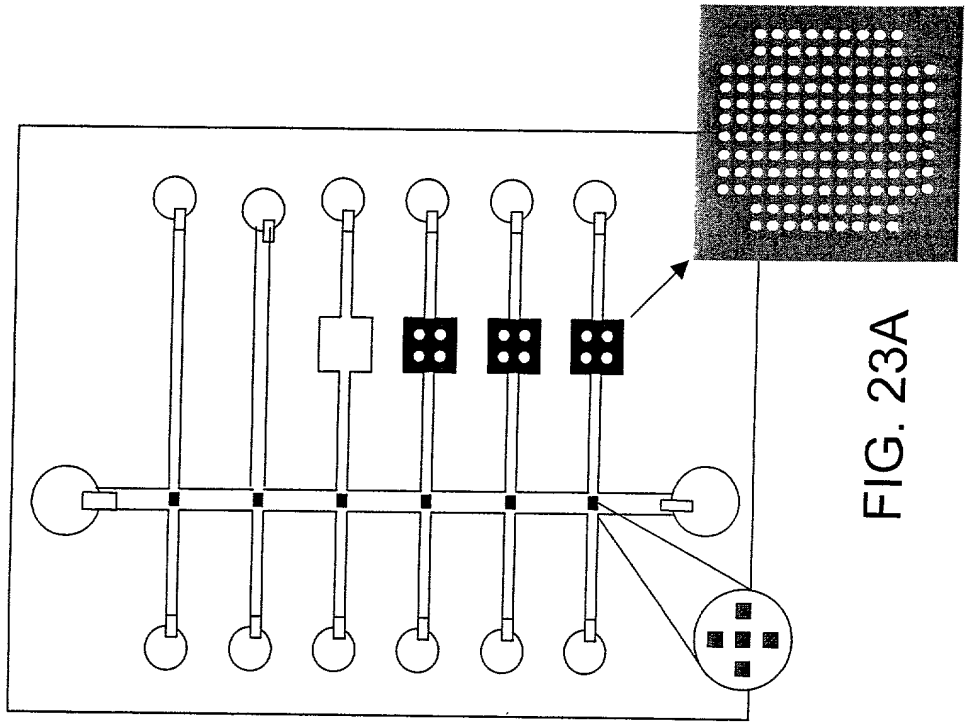
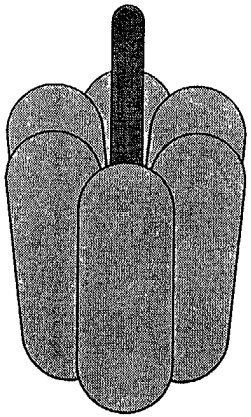


FIG. 23A

ATPase based Fluid-Micromixers



Cartoon of the multi-subunit enzyme – ATPase – that rotates in response to ATP synthesis to hydrolysis. The centrally located γ-subunit rotates relative to the hexameric α,β-subunit core.

FIG. 24A

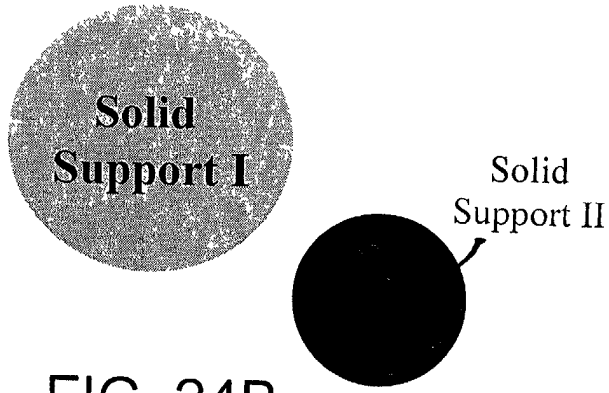
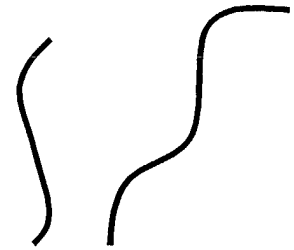


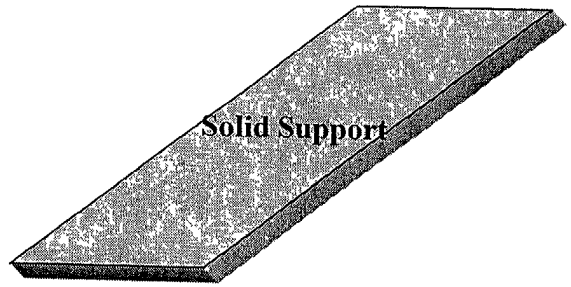
FIG. 24B

Spherical Beads as Solid supports for attaching different subunits of ATPase



Linkers for attaching different subunits of ATPase to the solid support

FIG. 24C



Flat platform base as Solid supports for attaching one of the subunits of ATPase

FIG. 24D

ATPase based Fluid-Micromixers, Model I

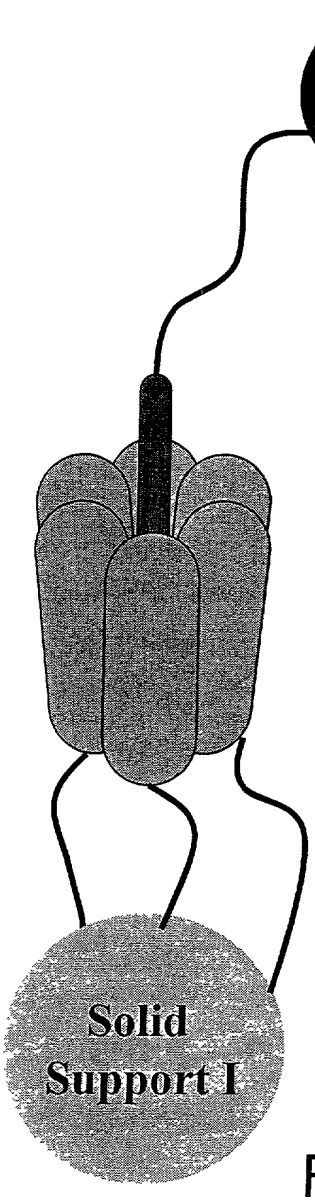
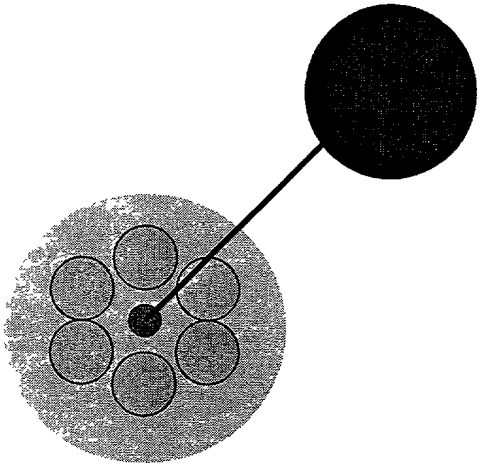


FIG. 25A

One particular implementation of ATPase-based fluid-micromixers. The γ-subunit and the α,β-subunit core are both attached to two different spherical beads.



A cartoon showing ATPase subunits attached to two beads from another angle.

FIG. 25B

A cartoon showing rotation of the two beads bound to ATPase (Model I micromixer) upon addition of ATP

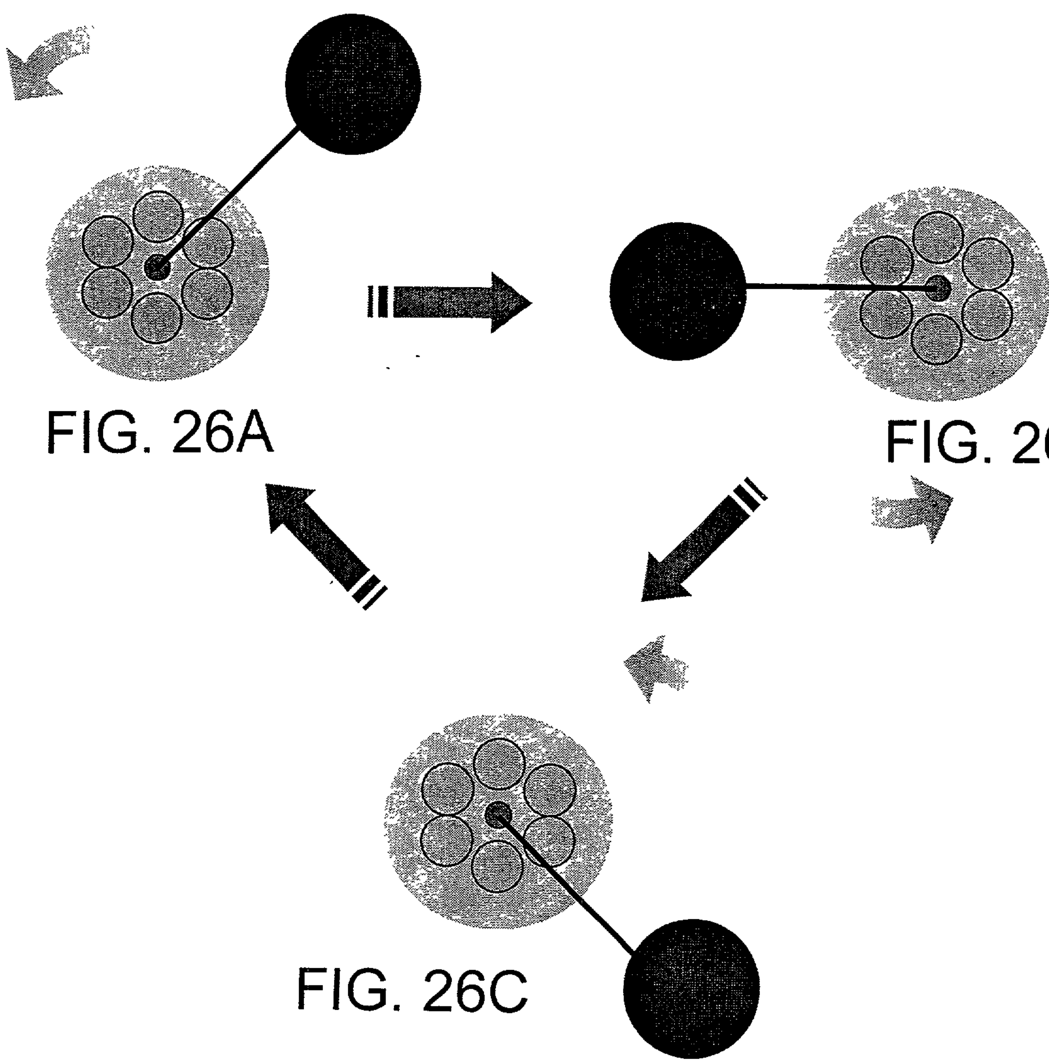


FIG. 26A

FIG. 26B

FIG. 26C

09996056 .032802

A cartoon showing multiple Model I Micromixers in action in a solution

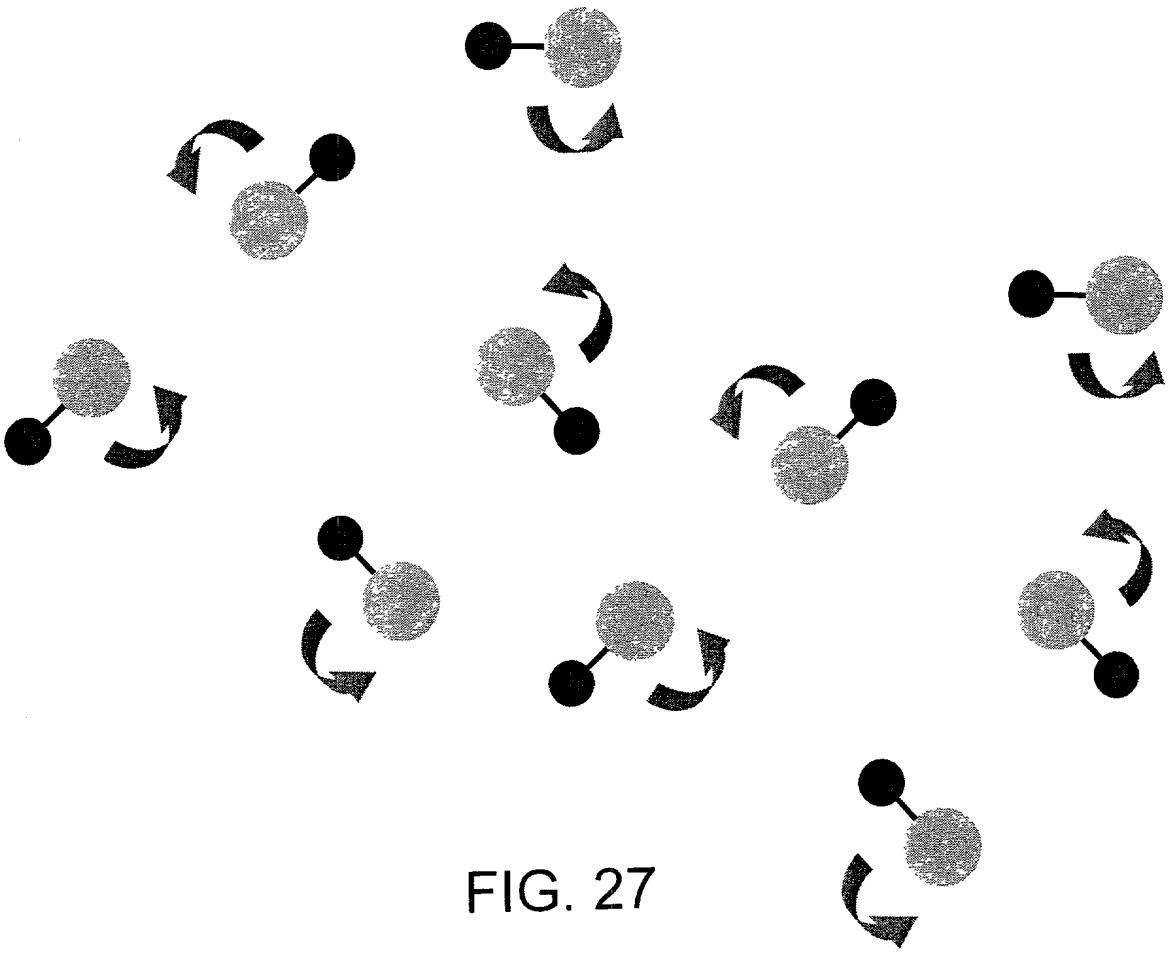
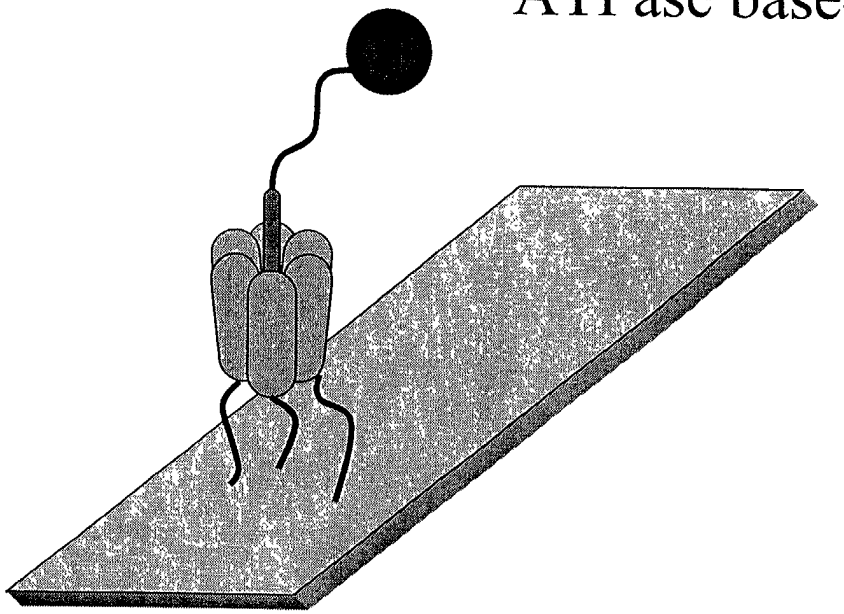


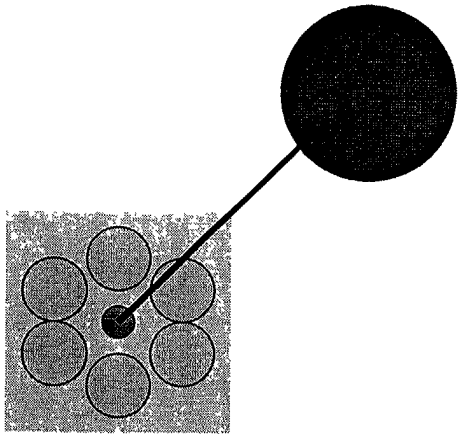
FIG. 27

ATPase based Fluid-Micromixers, Model II



Another implementation of ATPase-based fluid-micromixers. The γ-subunit is attached to a spherical bead and the α,β-subunit core is attached to a solid platform.

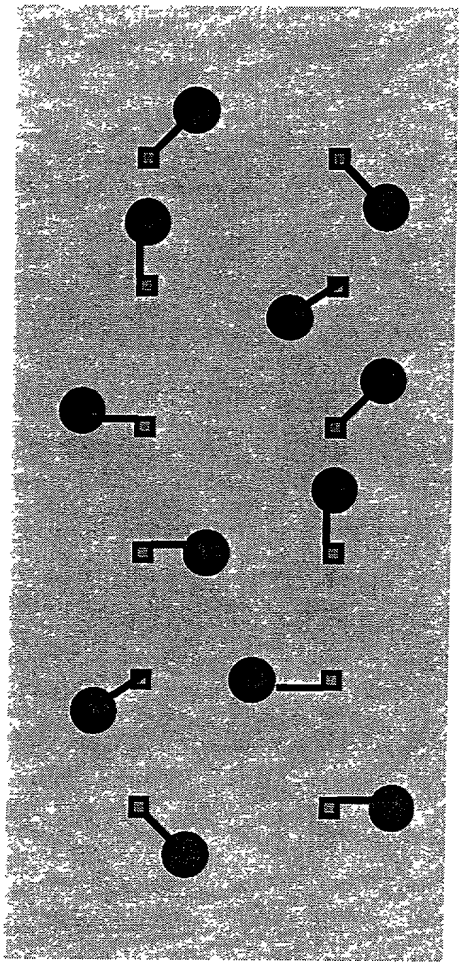
FIG. 28A



A cartoon showing ATPase subunits attached to two different surfaces from another angle.

FIG. 28B

A cartoon showing multiple Model II Micromixers in action in a solution



All the mixers are moving in a counter-clockwise direction

FIG. 29

09/996,056 - 12877-006001

Kinesin and Myosin based Fluid-Micromixers

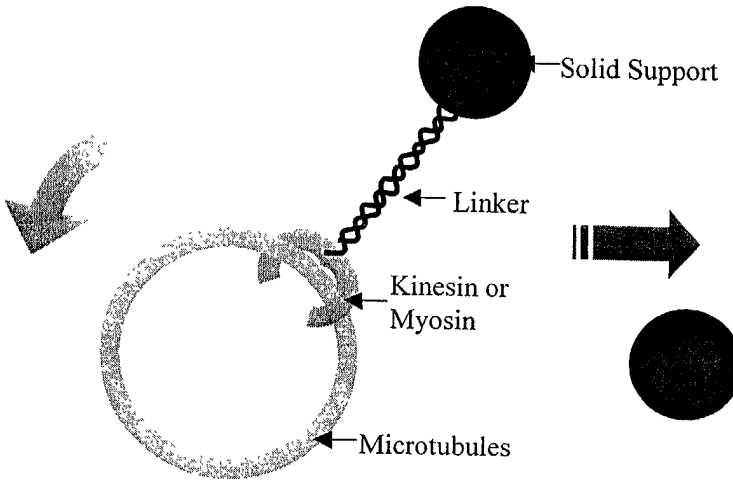


FIG. 30A

FIG. 30B

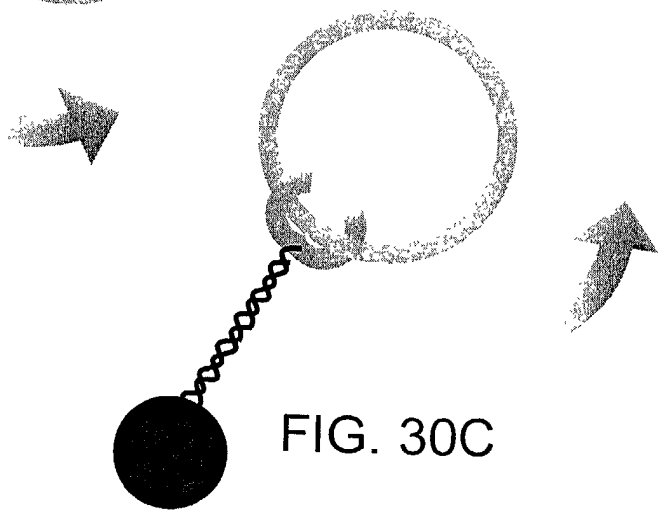


FIG. 30C

20020° 95096660

Circular Triplex Forming Oligo (CTFO) DNA and Other Pseudo-rotaxane based Fluid-Micromixers

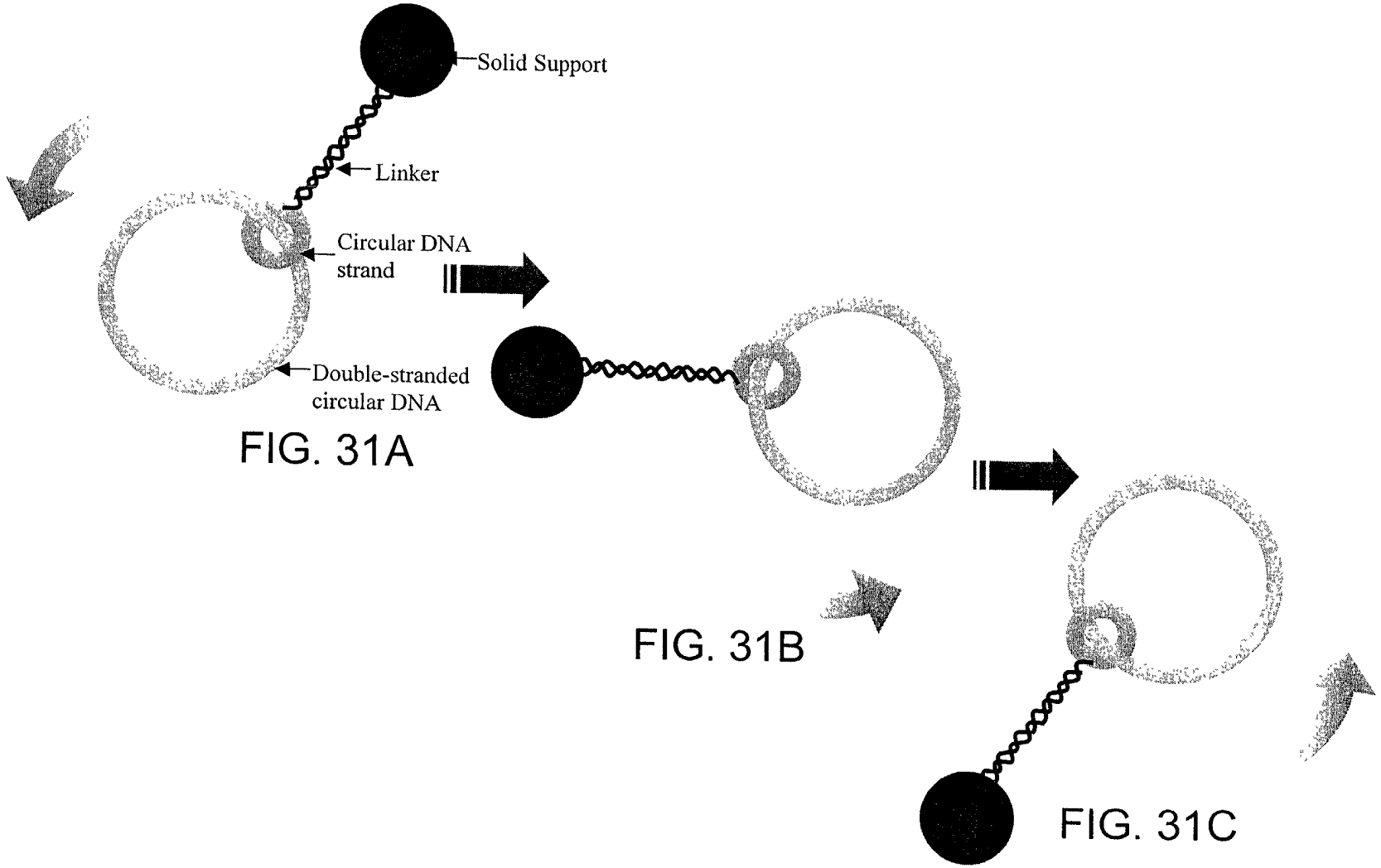


FIG. 31A

FIG. 31B

FIG. 31C

DNA Helicase and DNA Sliding Clamp based Fluid-Micromixers

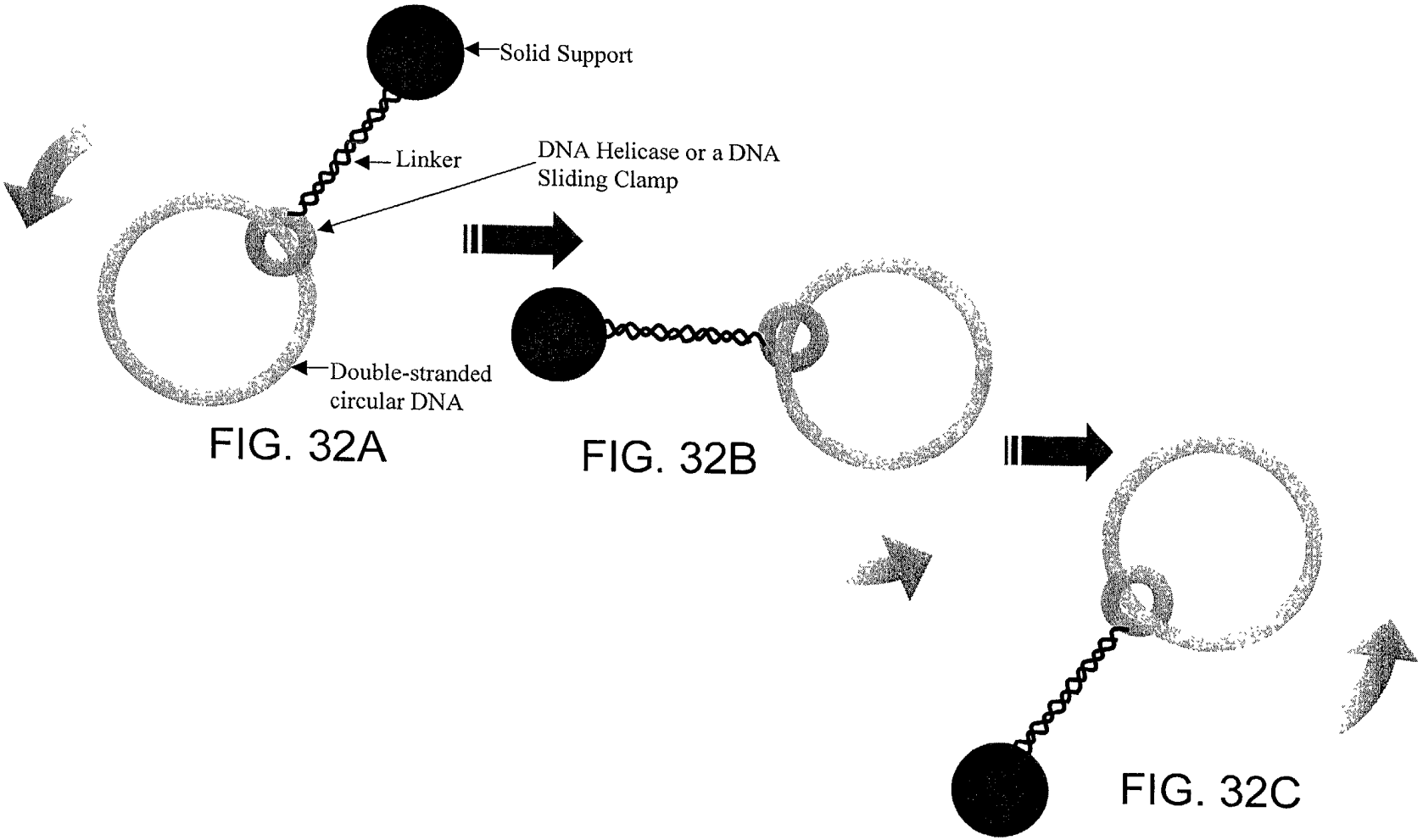


FIG. 32A

FIG. 32B

FIG. 32C

DNA Helicase (bound to Circular Triplex Forming Oligo (CTFO) or a Sliding Clamp) based Fluid-Micromixers

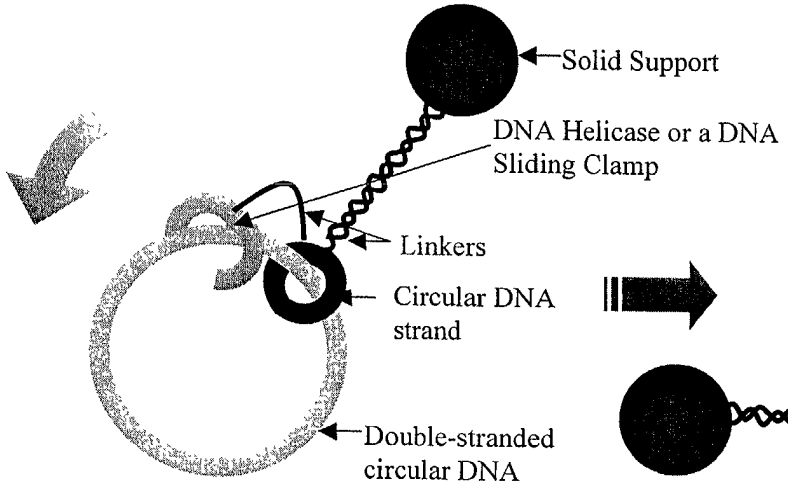


FIG. 33A

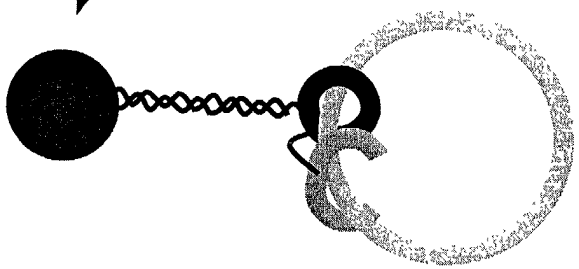


FIG. 33B

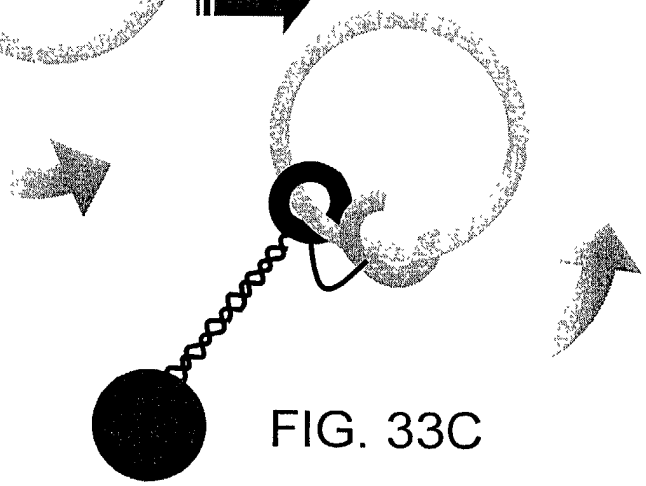
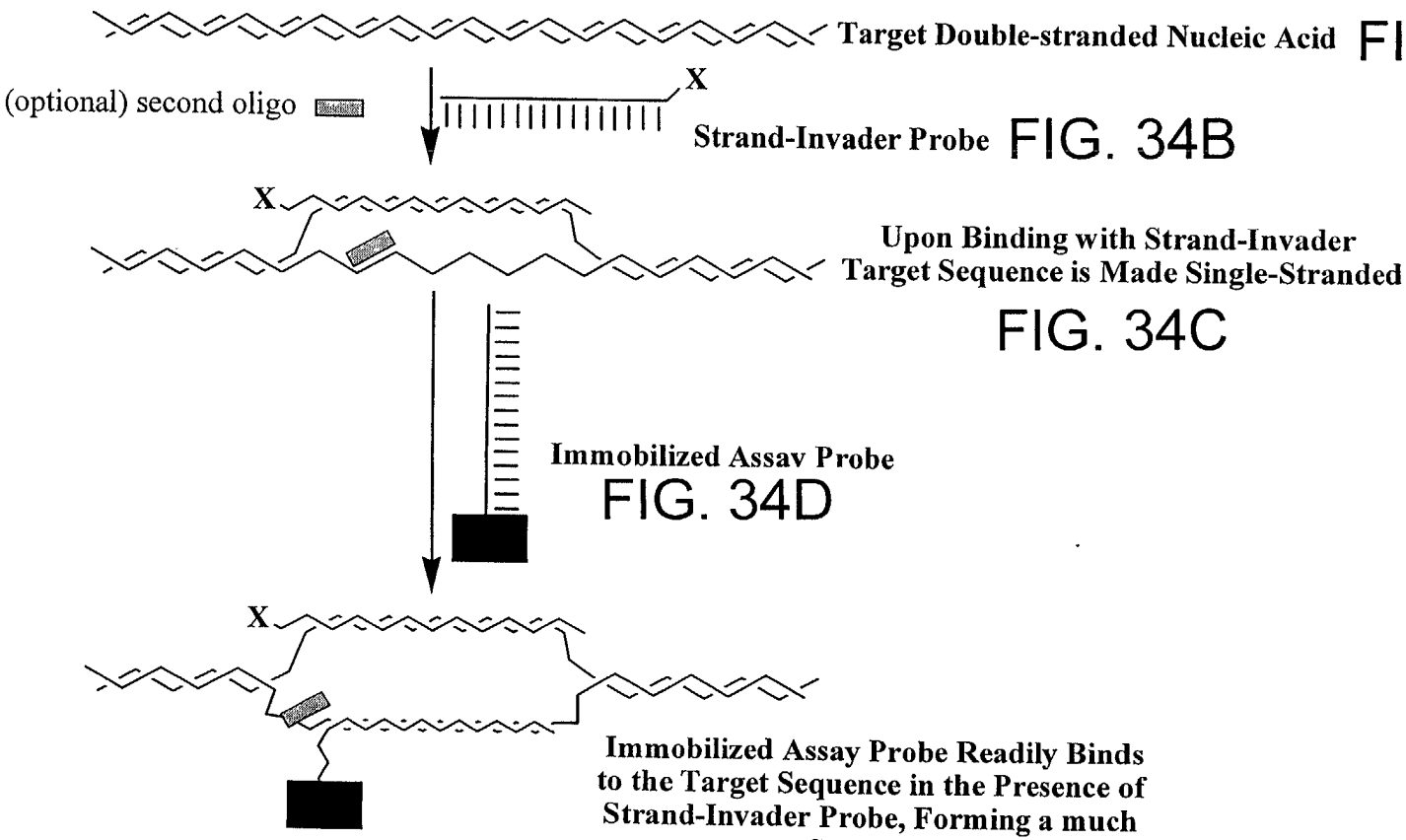


FIG. 33C

20020 95096660

Hybridization Enhancement Using Strand-Invader Molecules



A gasket/separator can be used in the current hybridization chambers to place two biochips facing each other in a single chamber for duplicate experiments.

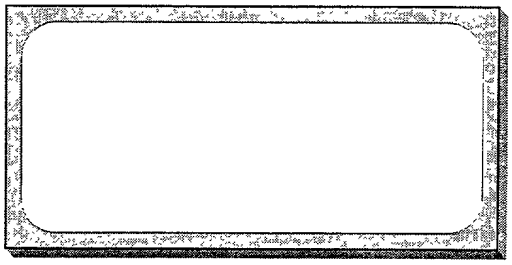


FIG. 35A

FIG. 35B

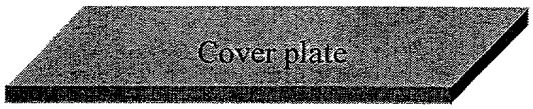


FIG. 35C

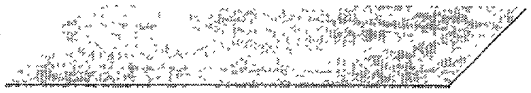


FIG. 35D

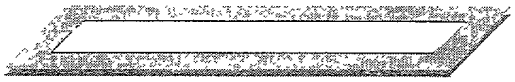
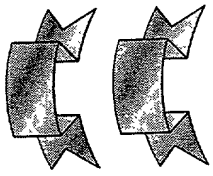


FIG. 35E

FIG. 35F

A sketch of one example of a new hybridization chamber. A hybridization chamber can be devised such that it fits two biochips.



Hybridization Chamber Clamps

FIG. 35G

I A gasket/separator can be used in the current hybridization chambers to place two biochips facing each other in a single chamber for duplicate experiments.

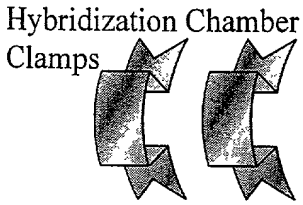


FIG. 36A

FIG. 36B

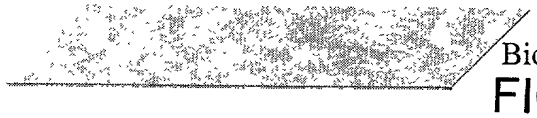


FIG. 36C

FIG. 36D

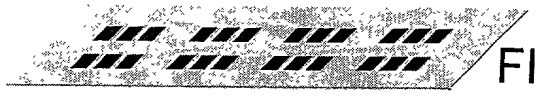


FIG. 36E

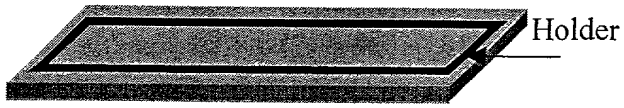


FIG. 36F

II The separator can also be built into the chamber.

FIG. 36G

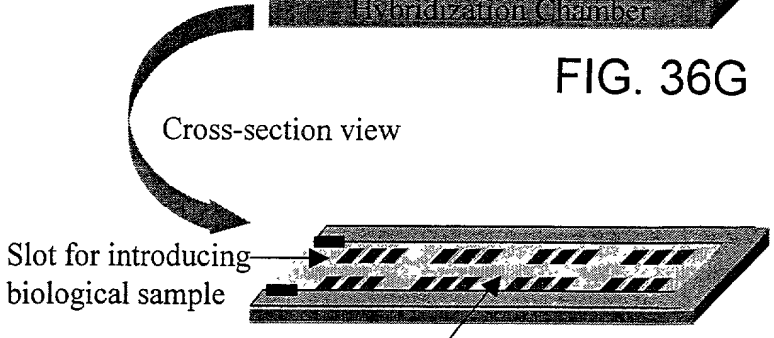
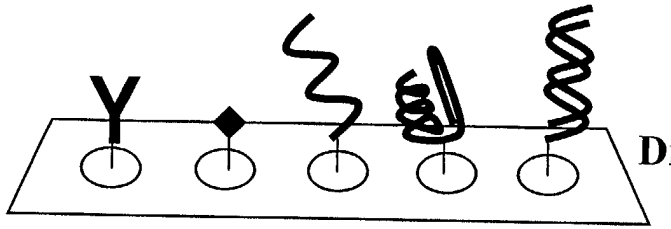


FIG. 36H

20020820 09096660



Different types of probes attached to the surface of a Biochip

FIG. 37A

Target Binding

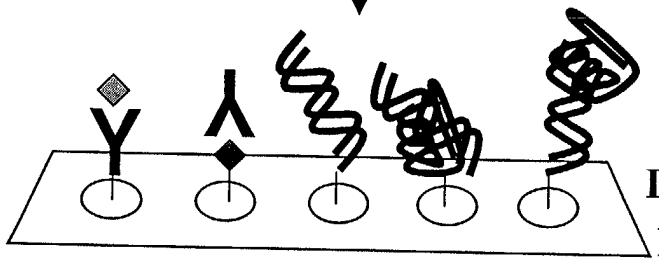


FIG. 37B

Different kinds of targets bound to probes on the surface of a Biochip

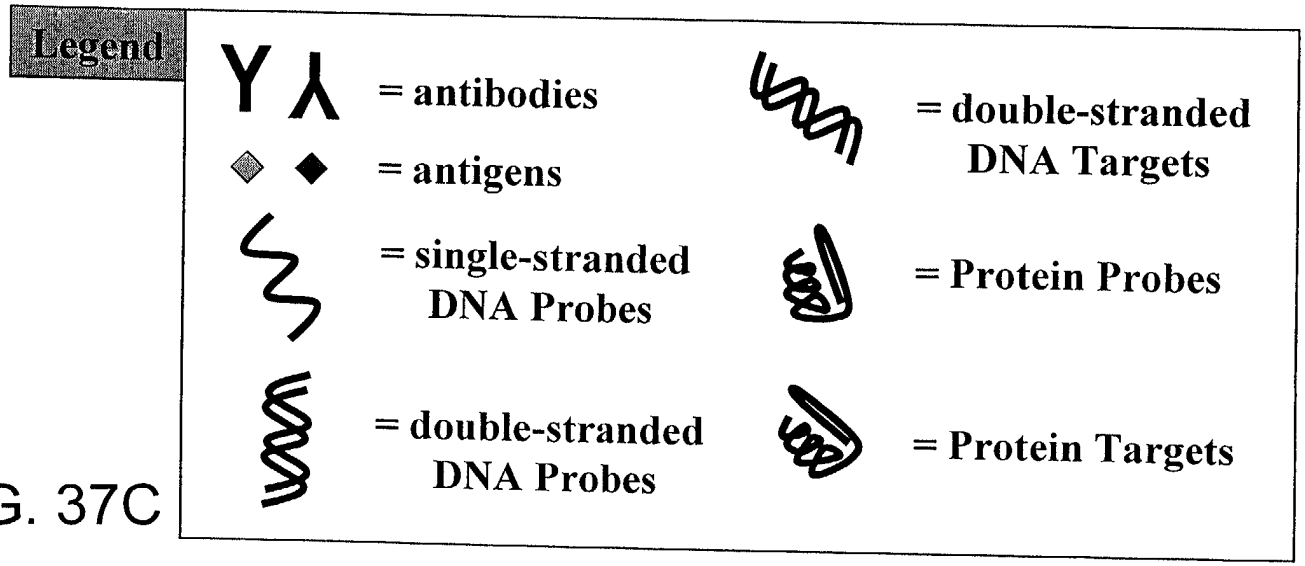


FIG. 37C